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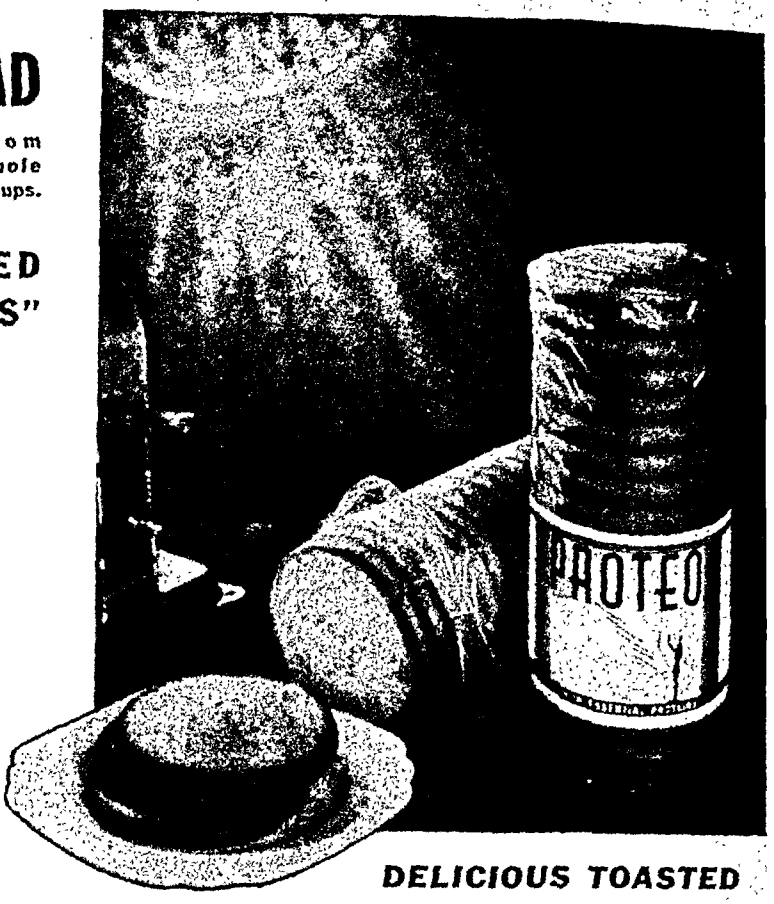
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CONTENTS

SECTION I.—CLINICAL MEDICINE — Page

AMEBIASIS AND AMEBIC DYSENTERY - - - - - - - - 4
Charles F. Craig, M.D., M.A., F.A.C.S., F.A.C.P.

AMEBIC DYSENTERY IN CHICAGO - - - - - - - - - 9
Herman N. Bundesen, M.D., Sc.D.

CERTAIN LATENT AND ATYPICAL TYPES OF AMEBIASIS - - - - - 10
Philip W. Brown, M.D.

MIGRAINE, AN ALLERGIC PHENOMENON - - - - - - - - 14
Albert F. R. Andresen, M.D., F.A.C.P.

DIAGNOSIS AND MANAGEMENT OF GALL TRACT, PARTICULARLY GALL-BLADDER, DISEASE - - - - - - - - - - - - - 18
B. B. Vincent Lyon, A.B., M.D., Sc.D.

GASTRIC ULCERS ASSOCIATED WITH CINCHOPHEN POISONING - - - 29
Leon Bloch, M.D. and David H. Rosenberg, M.D.

ABSTRACTS - - - - - - - - - - - - - - - 31

SECTION II.—EXPERIMENTAL PHYSIOLOGY

SYMPATHETIC SECRETORY INNERVATION OF THE GASTRIC MUCOSA - - - 36
Stewart G. Baxter

ROLE OF THE SYMPATHETIC NERVOUS SYSTEM IN GASTRIC SECRETION - - 40
Stewart G. Baxter

SECTION III.—NUTRITION

NUTRITION IN HEALTH AND DISEASE - - - - - - - - 44
Clifford J. Barborka, B.S., M.S., Sc.D., M.D.

SECTION IV.—ROENTGENOLOGY

WHY PEPTIC ULCERS ARE MISSED ON X-RAY EXAMINATION - - - - 52
Wm. H. Stewart, M.D., and H. Earl Illick, M.D.

SECTION V.—THERAPEUTICS

TREATMENT OF AMEBIC DYSENTERY - - - - - - - - 58
Horace W. Soper, M.D.

SECTION VI.—ABDOMINAL SURGERY

PRIMARY CARCINOMA OF LIVER IN INFANCY - - - - - - - 60
Ralph A. Kordenat, M.D.

ABSTRACTS - - - - - - - - - - - - - - - 63

SECTION VII.—SURGERY OF THE LOWER COLON AND OF THE RECTUM

UNUSUAL PROBLEMS IN PLASTIC SURGERY OF THE COLON - - - - 66
Jerome M. Lynch, M.D., F.A.C.S., and Vincent Hurly, M.D., F.R.C.S.E.

MULTIPLE FISSURES OF THE ANUS IN A CASE OF TERTIARY SYPHILIS - - 69
Louis A. Buie, M.D., and Winfield L. Butsch, M.D.

TUBERCULOUS ULCERATION OF THE RECTUM AND SIGMOID - - - - 70
Clement L. Martin, M.D.

SECTION VIII.—EDITORIAL

FOREWORD—BOARD OF GASTROENTEROLOGY—ENDAMEBIASIS IN THE UNITED STATES—FAMILIAL INCIDENCE OF PEPTIC ULCER - - - - - 72

SECTION IX.—BOOK REVIEWS

DISEASES OF THE DIGESTIVE TRACT - - - - - - - - 77
Arthur L. Bloomfield in Musser's Internal Medicine.

MYSTERY, MAGIC AND MEDICINE - - - - - - - - - 77
Howard W. Haggard

SECTION X.—AFTER HOURS

THE GOLD HEADED CANE - - - - - - - - - - 80
Anonymous

SOCIETIES, PROGRAMS AND PROCEEDINGS - - - - - - - 84

WHO'S WHO IN THE EDITORIAL COUNCIL - - - - - - - 88

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Section I.

Clinical Medicine: Digestive Diseases

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CHARLES F. CRAIG
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LEON BLOCH

AMERICAN JOURNAL OF
DIGESTIVE DISEASES
AND NUTRITION

AMEBIASIS AND AMEBIC DYSENTERY*

By

CHARLES F. CRAIG, M.D., M.A., F.A.C.S., F.A.C.P.†

NEW ORLEANS, LA.

THE occurrence of numerous cases of amebic dysentery in Chicago and throughout the United States in individuals who had visited Chicago has awakened much interest in an infection which is endemic in this country but which is usually unrecognized by the medical profession, especially in the Northern States. Unfortunately, the term "amebic dysentery" has become synonymous with amebiasis and both terms indicate to the average physician in this country a tropical disease of little general interest to the practitioner and one of rare occurrence.

In this lecture it is intended to discuss especially that symptom-complex of amebiasis known as "amebic dysentery", but before doing so it is essential that one have a clear conception of infection with *Endamoeba histolytica* and the meaning of the terms "amebiasis" and "amebic dysentery".

By the clinical term "amebiasis" is meant the invasion of the tissues of man by the pathogenic ameba, *Endamoeba histolytica*, the invasion occurring primarily through the mucous membrane of the large intestine, which may be followed by symptoms varying all the way from slight digestive disturbances to the most severe symptoms of amebic dystentery or amebic abscess of the liver or other organs. By the term "amebic dysentery" is meant a symptom-complex, characterized by a bloody, mucoid diarrhoea caused by *Endamoeba histolytica* and occurring as one of the clinical manifestations of amebiasis.

From these definitions it will be noted that amebic dysentery is simply a part of the clinical picture of amebiasis and it should be borne in mind that while amebiasis is a common infection in the United States, amebic dysentery is comparatively rare, although it undoubtedly occurs much more frequently than Health Returns would indicate. The recognition of the fact that *amebic dysentery is not a disease entity but is a part only of the picture of amebiasis is essential* to a proper understanding of amebic infection and until this fact is recognized we will continue to have erroneous ideas regarding the prevalence and nature of this infection in the United States.

It is unnecessary here to do more than review very briefly the HISTORY of amebiasis and amebic dysentery. Curiously enough, although this infection, even now, is thought of as a tropical disease, the discovery of the parasite causing amebic dysentery, and the first description of the lesions caused by it, was made by Lösch, in 1875, in a patient suffering from dysentery observed in St. Petersburg, Russia. His work was confirmed by Kartulis (1886) and Hlava (1887) and, in the United States by Osler (1890), Stengel (1890), Musser (1891) and Dock (1891). In 1903, Huber and Schaudinn definitely differentiated *Endamoeba histolytica* from the non-pathogenic *Endamoeba coli* and in 1913, Walker and Sellards proved conclusively by experiments upon human volunteers that *Endamoeba histolytica* is the cause of amebic dysentery. Since the observations referred to above several other species of amebae have been found to live in the intestine of man and today we accept five species, i.e., the pathogenic *Endamoeba histolytica* and the non-pathogenic *Endamoeba coli, Endolimax nana, Iodamoeba bütschlii* and *Dientamoeba fragilis*.

The GEOGRAPHICAL DISTRIBUTION of amebiasis is world-wide, for wherever *Endamoeba histolytica* has been looked for it has been found in a considerable proportion of the individuals examined. The infection is more prevalent in the tropics but surveys have shown a very high degree of prevalence in poorly sanitated rural regions in this country. Wherever sanitation and personal hygiene is poor amebiasis is very prevalent, whether in the tropics, sub-tropics or the temperate zones. While this is true, amebic dysentery is much more prevalent in warm countries than in cold countries, in my opinion largely due to the greater resistance to the infection in the inhabitants of cold countries and, also, the lesser chances of heavy infection. In the United States amebic dysentery has been reported from practically every state in the Union, but it is more often observed in the southern states than in the northern states. There can be little doubt that many cases of amebic dysentery are wrongly diagnosed annually and that this type of dysentery is much more prevalent than is usually believed. However, the vast majority of individuals infected with *Endamoeba histolytica* in this country do not develop amebic dysentery, whereas in tropical countries, except in native races who apparently develop some immunity to this symptom-complex, a considerable proportion of infected individuals develop dysentery.

The INCIDENCE OF INFECTION with *Endamoeba histolytica* varies greatly and the figures given in the literature must be interpreted according to the methods used in making the various surveys. Dobell (1917) has shown that the examination of a single unstained preparation demonstrates not more than one-third of the actual infections, while three such examinations demonstrate between one-half to two-thirds. Since Dobell's work improved methods for the demonstration of this parasite have been evolved, as the examination of concentrated specimens and the use of cultures, and by making use of these methods the number of examinations may be cut down and their accuracy increased. Space forbids consideration of the incidence of infection with this parasite outside the limits of the United States but in this country it has been shown that the incidence varies from less than one per cent in some localities to as high as 38 per cent in others. In the examination of food handlers in hotels in Chicago, Tonney, Hoeft and Spector (1933) found 7.1 per cent infected in one hotel, while a later publication by Bundesen,

*The Second Jessie Horton Koessler Lecture delivered before the Institute of Medicine in Chicago, January 26th, 1934.

†Colonel, U. S. Army. Retired. Professor of Tropical Medicine and Director of the Department of Tropical Medicine, School of Medicine of the Tulane University of Louisiana, New Orleans, Louisiana.

Rawlings and Fishbein (1933) records an incidence of 18.6 per cent in the same hotel after further examinations. Faust (1930) found an incidence of 20 per cent in Wise County, Virginia, while Meleney, Bishop and Leathers (1932) in an examination of 20,237 individuals in Tennessee, found this parasite in 2,305, or 11.4 per cent, and state it is their belief that had repeated examinations of these individuals been made the percentage would have been twice that, or 22.8 per cent.

Up to the present time no nation-wide survey of the incidence of *Endamoeba histolytica* has been made in this country, but enough has been accomplished in this line to demonstrate that it is conservative to estimate that somewhere between 5 and 10 per cent of the population of the United States harbor this parasite. As the parasite is one that lives in the tissues of man and probably produces lesions in all cases, so far as is shown by available evidence, amebiasis becomes a public health problem worthy of the most serious consideration.

THE LIFE HISTORY of *Endamoeba histolytica* is a simple one. The organism belongs to the Protozoa, or single-celled animals, and has three stages in its life cycle in man. In the tissues of the intestine and in other tissues, as well as in the feces during diarrhoea or dysentery, it occurs as a motile trophozoite, showing active progressive motility by means of pseudopodia formed of the ectoplasm that are projected from the periphery of the parasite and into which the endoplasm flows, thus resulting in a change of position and motility. In the lumen of the intestine these motile forms also occur but do not usually appear in the feces unless the stools are fluid or semi-fluid in consistence. Under certain conditions in the intestine the motile trophozoites round up and become motionless at which time they are known as pre-cystic forms, and these, in turn, become cysts, which are voided in semi-formed and formed stools. In the motile forms, division occurs by simple fission into two amebae, no reproduction occurs in the pre-cystic forms, and in the cysts the nucleus divides into four nuclei, and cysts are found in the stools containing from one to four nuclei, the fully developed cyst having four. These cysts are voided in the feces and if they reach the food or drink of man, are swallowed, pass through the stomach and small intestine, and excyst, liberating in the upper portion of the large intestine, a four-nucleated ameba, which, after a complicated series of nuclear changes divides into eight small amebae. These amebae may then invade the walls of the intestine or may again encyst.

THE METHODS OF TRANSMISSION of *Endamoeba histolytica* depend upon the fact that the cysts are the infecting agents and that man is infected by food or drink contaminated with feces containing the cysts. Under normal conditions, the motile trophozoites of this parasite cannot infect man for the reason that they are destroyed by the gastric juice so that it follows that patients suffering from acute amebic dysentery or diarrhoea are not concerned in the transmission of the infection, as cysts are not present in diarrhoeal or dysenteric stools. It is the individual who is apparently healthy, or who has recovered from amebic diarrhoea or dysentery, or has other symptoms of the infection, who is a source of infection to those about him, as the cysts occur in semi-formed or formed stools. As practically *all untreated or improperly treated cases of amebic diarrhoea or dysentery become carriers of the cysts* of this parasite, it is obvious that they all are potential sources of infection to others. Carriers also arise from infection from other carriers and it is these individuals who are apparently healthy, or have mild symptoms of the infection, without diarrhoea or dysentery, who are most active in transmitting the infection to those about them.

Amebiasis and amebic dysentery may be transmitted to man through a water supply polluted with feces containing the cysts; through the use of human excreta in the fertilization of garden vegetables; through the droppings of flies and through the handling of food and drink by infected individuals who are excreting the cysts of the parasite in their feces.

Infection through a *contaminated water supply* is a common method in localities where there is no properly impounded and filtered water supply and where the inhabitants depend upon wells, springs, and tanks for water. It has been shown by many observers that the cysts of *Endamoeba histolytica* may live for days and even weeks in water, depending upon the temperature and the number of bacteria present. This method of transmission is of comparatively little importance in this country except in rural districts where soil pollution is practiced and wells and springs are used as a source of the water supply.

The *use of human excreta in the fertilization* of vegetable gardens, as practiced so widely in the Orient and to some extent in this country, despite laws to the contrary, is an important method of transmisison. The cysts of this parasite will remain alive in moist fecal material for as long as two weeks according to the experimental evidence available, so that the danger of transmission from excreta used in the manner mentioned is obvious.

The contamination of food and drink by the droppings of flies is sometimes a method of transmission of amebiasis where flies are very plentiful, individuals are collected in large numbers within a small area, and food-stuffs are unprotected from these insects. The cysts of *Endamoeba histolytica* remain viable in the intestine of flies for as long as 48 hours during which time the droppings of the insect contain them and food may be thus contaminated. In 1916, I observed an outbreak of amebic dysentery on the Mexican Border which was believed to have been caused by flies, and it is in such conditions as the concentration of troops in camps where flies are prevalent that one may expect some transmission of the infection through these insects.

In otherwise well-sanitated districts, the most common method of transmission of this parasite is through *the contamination of food and drink by food handlers* who are carriers of this ameba. In cities and towns having an impounded water supply and where sanitation is otherwise excellent, food handlers employed in hotels, restaurants, lunch counters and roadside refreshment stands, are the chief source and transmitters of amebic infection. The transmission of the infection by food handlers is practically a certainty unless the greatest care is taken regarding personal hygiene and the cleanliness of the hands of all who handle food. The incidence of infection in food handlers employed in public eating places is often very high, due to their close association and the constant intake of the cysts in food which they themselves contaminate, and one infected food handler may infect many others with whom he is associated until the vast majority of the food handlers in a particular institution may show infection.

Other methods of transmission of this infection will suggest themselves but those mentioned are of practical significance. Of those mentioned, it is believed that the food handler, by and large, is of the greatest importance as a source of amebiasis.

The question of the occurrence of *epidemics of amebic dysentery* and of the possible *existence of avirulent and virulent strains* of the parasite demand brief mention. It is well known that amebic dysentery usually occurs in the form of sporadic cases, but, under certain conditions, it may occur in an epidemic form, if by epidemic is meant the occurrence of many cases within a limited period of time. In the early days of the Philippine Insurrection, we observed many outbreaks of this type of dysentery among our troops operating in the field, and the possible confu-

sion with bacillary dysentery was disposed of by the fact that agglutination reactions and cultures were made for the dysentery bacilli with negative results, while the stools of these cases swarmed with motile trophozoites. At autopsy, in those dying of the infection, the typical lesions of amebic dysentery were shown. In such outbreaks, several men in one company would go on "sick report" with this type of dysentery within a short period of time. It is believed that these epidemic-like outbreaks of amebic dysentery were due to the great lessening of resistance in the soldiers brought about by continual exposure to extremes of temperature, constant wetting by the heavy tropical rains, insufficient or unsuitable food, constant reinfection by swallowing numerous cysts in badly contaminated water, and the mental strain and depression in home-sick men operating in the field against a cunning and cruel foe. Under such conditions, resistance must inevitably be greatly reduced and many cases of amebic dysentery will occur within short periods of time. In 1916, in the epidemic I observed in troops camped at El Paso, Texas, a total of 118 cases of amebic dysentery occurred in the period between July 1st, 1916, and November 1st, 1916. In every one of these cases agglutination reactions and cultures were made for the dysentery bacilli with negative results, while *Endamoeba histolytica* trophozoites were numerous in every case. I believe that such evidence demonstrates that, under conditions greatly depressing natural resistance, or where massive doses of cysts are ingested, amebic dysentery may occur in epidemic form.

The question of the existence of strains of *Endamoeba histolytica* differing in virulence is one that is often raised and is of great practical importance. It may be answered at the present time by the statement that while some evidence has been brought forward favoring such variations in virulence in kittens, notably by Meleney and Frye (1933), it is not sufficient to negate the large amount of experimental evidence furnished by other observers that apparently demonstrates that there is no difference in virulence between strains isolated from symptomless carriers and those suffering from severe attacks of amebic dysentery. It should be remembered that in all of Walker and Sellards (1913) successful experiments in producing amebic dysentery by the feeding of the material containing *Endamoeba histolytica* to human volunteers, the cysts used originated from symptomless carriers of this parasite.

The PATHOLOGY OF AMEBIASIS AND AMEBIC DYSENTERY is characteristic but space forbids a discussion of the lesions which are observed. The lesions are caused, so far as we know, by the combined *cytolytic action* of the parasite, *its capability of penetrating the cytolysed tissues* by virtue of its amoeboid motility, and by the *secondary invasions of the tissues by bacteria present in the intestine.* In lesions in which there is no secondary bacterial infection, there is little evidence of inflammatory reaction, the amebae lying in groups or singly, surrounded by small areas of granular matter representing the cytolysed tissue, while polymorphonuclear leukocytes are absent or very few in number. I desire to stress the fact that macroscopical amebic ulcers may be present in the intestine of symptomless carriers of *Endamoeba histolytica* and that amebic abscess of the liver may occur in individuals who have no diarrhoea or dysentery. The observations of Kessel, (1928), Hegner, Johnson and Stabler (1932) and of Craig and Kagy (1933) upon amebiasis in kittens, monkeys and dogs, demonstrate that marked amebic ulceration may occur in the intestine of these animals without the production of symptoms of dysentery, while those of Councilman and Lafleur (1890), Dock (1891), Musgrave (1910), Bartlett (1917), and Hiyeda and Suzuki (1932), demonstrate that marked amebic ulceration may exist in the intestine of man without producing symptoms of severe diarrhoea or dysentery. I have observed many instances in which amebic ulcerations were found at *postmortem* in patients dying from other disease conditions and in whom there had been no symptoms of dysentery while they were under observation.

In discussing the SYMPTOMATOLOGY of amebiasis I shall discuss that of the symptom-complex known as "amebic dysentery" only, but it should be remembered that the vast majority of individuals infected with *Endamoeba histolytica* in this country do not present the symptoms of amebic dysentery but exhibit a host of symptoms connected with the gastro-intestinal tract and the nervous system, with constipation and attacks of diarrhoea alternating in many instances. The more spectacular series of symptoms known as "amebic dysentery" forcibly attracts the attention of the medical profession, as in the present outbreak of this condition, but it always should be borne in mind that cases exhibiting these symptoms are very rare as compared with the hundreds and thousands of individuals who have symptoms due to the invasion of the intestine by this parasite. Each one of these individuals is liable to develop amebic dysentery and hence the great practical importance of early recognition and proper treatment of the infection.

The PERIOD OF INCUBATION OF AMEBIC DYSENTERY is unknown in the vast majority of infections. This can be readily understood when one realizes that *Endamoeba histolytica* may live in the tissues of the intestine for months and years without producing symptoms of dysentery and that one never knows, except under experimental conditions, just when his infection may have been contracted. In an infection as widespread as the present, one can never be sure when his infection occurred unless his stools happen to have been examined and found negative shortly before the onset of symptoms, and even in such cases one could never be sure of the *exact* period of incubation. So far as I know, the only definite experimental evidence that we posesss upon this point are the results of Walker and Sellards (1913) in the production of amebic dysentery in human volunteers. In the 4 cases of dysentery experimentally produced by feeding the cysts of *Endamoeba histolytica,* the incubation periods from the time of feeding to the onset of symptoms of dysentery were 20, 57, 87, and 95 days respectively, with an average period of 64.8 days. These figures show how absurd it is to endeavor to state the period of incubation of amebic dysentery within limits usually implied in our understanding of the term.

The symptoms which we recognize as those of "amebic dysentery" differ markedly in different individuals, in some assuming a fulminant character followed by death in a comparatively short time, while in others they may be very mild and rapid spontaneous recovery may occur. The onset may be sudden but more frequently it follows repeated attacks of diarrhoea and often is preceded by a diarrhoea. Where the onset is sudden, the patient is acutely seized with severe abdominal pain, this sometimes accompanied by nausea or vomiting, and sometimes by chilly sensations or a distinct chill. There is an intense desire to defecate, the first stools passed being formed or semi-formed, but succeeding stools rapidly become semi-fluid or fluid until finally small amounts of material composed almost entirely of blood-stained mucus and necrotic shreds of the mucous membrane are passed with considerable tenesmus. The number of bowel movements varies from 6 to 8 in 24 hours in the mild cases, to as many as 30 to 40 in the most severe infections, the average number being from 15 to 20 in 24 hours in well-marked cases of amebic dysentery. The patient may become rapidly exhausted, complains of aching in the lumbar region, of great weakness in the legs, and is mentally depressed. In the milder attacks, fever is not present but in severe attacks it may register from 100 to 102 F. and is usually higher in

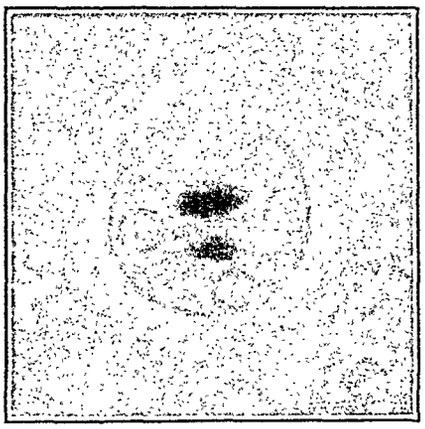


Figure 3.

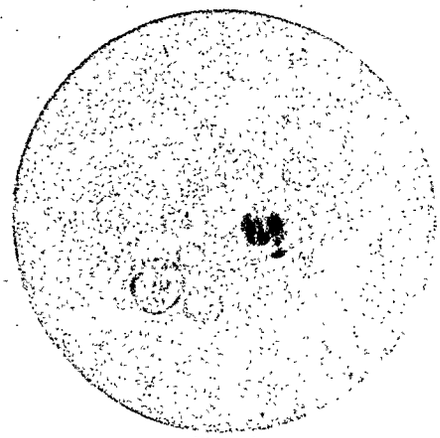


Figure 1.



Figure 2.

Figure 1. Trophozoite of *Endameba histolytica*. Note nucleus, ingested amorphous material, and numerous red blood corpuscles. Stained with iron-hematoxylin.

Figure 2. Trophozoites of *Endameba histolytica*, the one on the left showing three short pseudopodia. Stained with iron-hematoxylin.

Figure 3. Cyst of *Endameba histolytica*. Three nuclei are visible chromatoidal masses. Stained with iron-hematoxylin.

(From the Army Medical Museum Collection, Washington, D. C.)

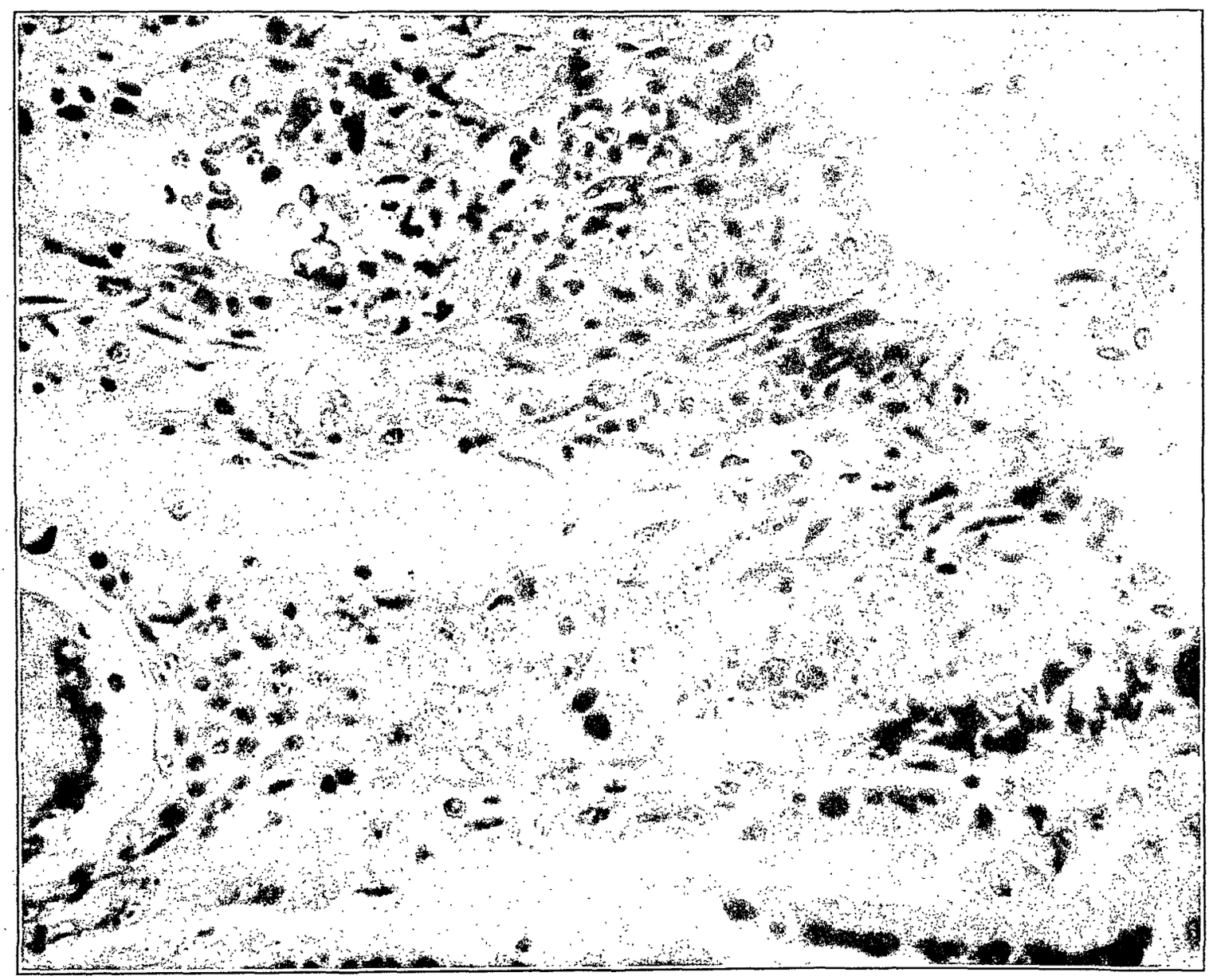


Figure 4.

Figure 4. Section of intestine showing *Endameba histolytica* just entering the mucous coat and some within and between the glands. This condition is probably present in most carriers of this parasite who have no symptoms and represents the earliest stage of invasion of the ameba. (From the Army Medical Museum Collection, Washington, D. C.)



Figure 5

Section of intestine showing *Endameba histolytica* in the submucous and muscular coats. X475. (From the Army Medical Museum Collection, Washington, D. C.)

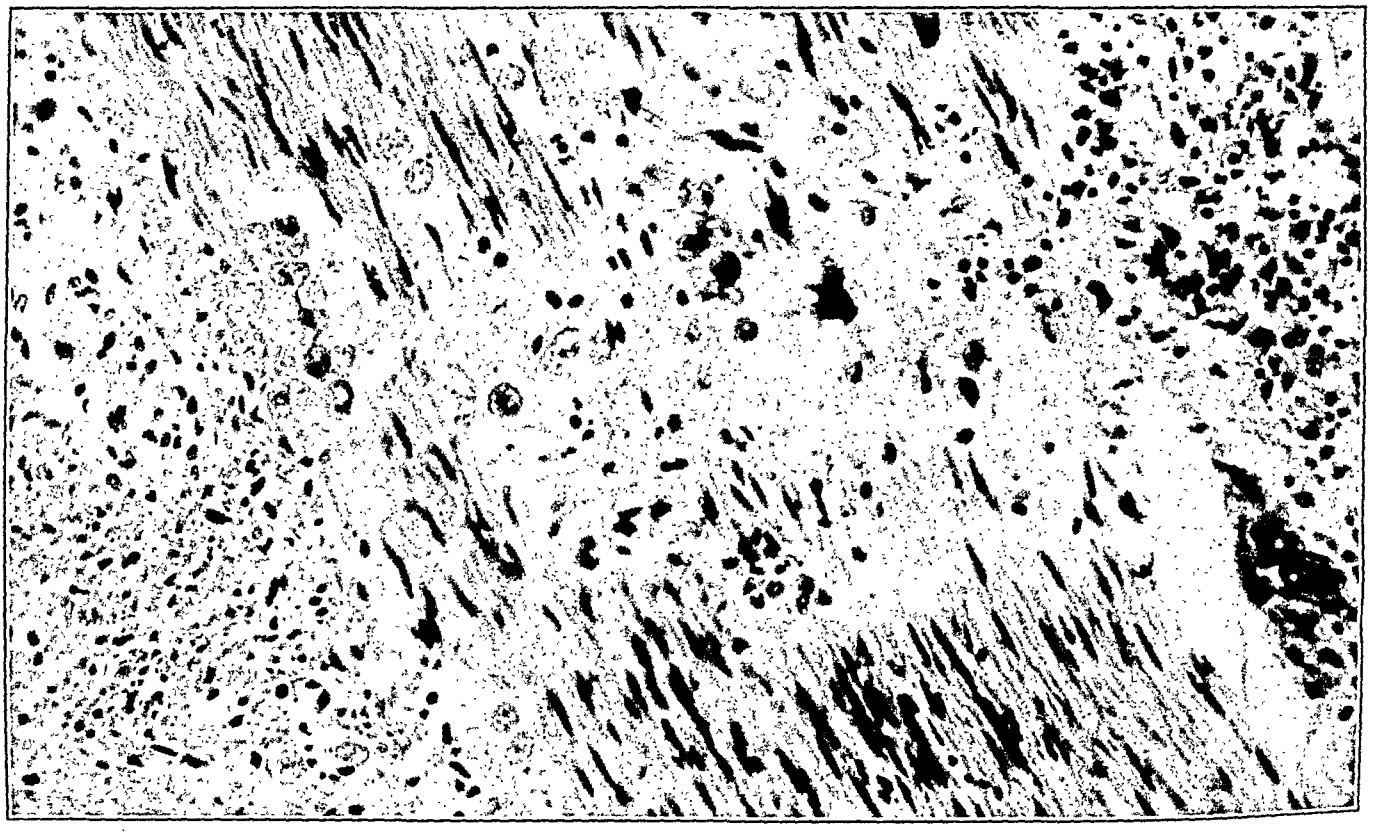


Figure 6.

Section of intestine showing invasion of the muscular coat by *Endameba histolytica*. Note the cytolysis of the muscle fibres and the absence of inflammatory reaction. X375. (From the Army Medical Museum Collection, Washington, D. C.)

the fulminant attacks. The impression that fever never occurs in amebic dysentery is incorrect, as it is not infrequently observed, but it is not so high and not so universally observed as it is in the bacillary types of dysentery. Toxaemic symptoms are not so severe or so often observed as in bacillary dysentery unless there is a mixed infection.

If the onset is gradual, following diarrhoeal attacks, the symptoms are similar. The so-called "gangrenous" and "fulminating" types of amebic dysentery are fortunately rare. They are characterized by sudden onset, extreme early prostration, fever, an excessive number of bowel movements containing much mucus, blood and sloughs or shreds of necrotic tissue, and evidences of severe toxemia. Death may occur in from 5 to 10 days after onset. Usually it is due to cardiac collapse from exhaustion and toxemia. I believe that all such cases of so-called amebic dysentery are really mixed infections with one of the dysentery bacilli, with pyogenic cocci, or other bacteria.

The PHYSICAL SIGNS present during an attack of acute amebic dysentery are: tenderness of the abdomen, especially over the cecum, ascending or descending colon; a sallow appearance of the skin which may be slightly jaundiced if a hepatitis is present and rapid emaciation in the severe cases. The tongue is usually coated with a yellowish brown fur, the breath is foul and labial herpes may occur if fever is present. Some patients will complain of tenderness and slight pain in the hepatic area and when this occurs it always indicates the presence of a hepatitis and possible commencing abscess formation in the liver.

Spontaneous symptomatic recovery usually occurs after the first acute attack of amebic dysentery and, very rarely, complete recovery may occur, but most patients, after a period of constipation or constipation alternating with diarrhoea, have an exacerbation of the acute dysenteric symptoms. This condition of alternating constipation and dysentery known as "chronic amebic dysentery", may last for many years and result in a condition of chronic invalidism. It is in such long-continued infections, accompanied by dysenteric attacks, that the colon may become so thickened that it may sometimes be palpated as a dougheyfeeling tube in localized areas or for almost its entire course in the abdomen.

The BLOOD PICTURE in acute amebic dysentery is not characteristic. There may be a slight anemia and a somewhat greater relative reduction in hemoglobin, while the leukocyte count ranges from normal in mild cases to from 12,000 to 20,000 leukocytes per cu. mm. in severe cases. In chronic amebic dysentery there is usually an anemia, the red cell count varying between 3,500,000 to 4,000,000 cells per cu. mm. in the average case, but it may fall as low as 2,000,000 just before death. A slight leukocytosis usually is present, and some authorities state that an *eosinophilia* occurs but this has not been my experience in either acute or chronic dysentery.

The DIAGNOSIS of amebic dysentery must depend upon the demonstration of *Endamoeba histolytica* in the stools of the patient. The symptoms and physical signs enumerated, even in the most typical attack of amebic dysentery, are not pathognomonic. This type of dysentery cannot be differentiated from some types of bacillary dysentery except by a study of the stools and the demonstration of the parasite. In *acute amebic dysentery*, the diagnosis rests upon finding the actively motile trophozoites of the parasite, while in the *quiescent periods* between active dysenteric symptoms in *chronic cases*, and in carriers, with or without symptoms, the diagnosis rests upon finding the cysts of the parisite in the semi-formed or formed stools.

Unfortunately, comparatively few laboratory technicians and physicians, at the present time, are capable of differentiating the five different species of amebae living in the human intestine, so that the diagnosis of amebiasis and amebic dysentery is much handicapped because of the lack of trained personnel. This fact cannot be lightly regarded and calls for correction by the training of sufficient personnel. I have no hesitation in stating that the diagnosis of amebic dysentery, of amebic diarrhoea and of the carriers of this parasite *demands, in every case, the demonstration of Endamoeba histolytica in the feces* of the suspected individual, and that the attempt to differentiate amebic and bacillary dysentery, on clinical symptoms alone, has lead to the greatest confusion in our statistics regarding the relative incidence of these infections throughout the world. It should also be remembered that amebic and bacillary dysentery may coexist and that in many cases of bacillary dysentery *Endamoeba histolytica* may be found and yet have nothing to do with the clinical picture. If possible, *agglutination tests* and *cultures* for the various types of dysentery bacilli should be made even though the ameba may be found in the patient's stools.

For the demonstration of *Endamoeba histolytica*, we have the direct microscopical examination of the feces, using both stained and unstained perparations; the use of cultivation methods for the parasite; the use of concentration methods if cysts are to be searched for; and the use of the complement fixation test. Simple microscopical examination of fresh, unstained preparations, is successful in the vast majority of cases of acute amebic dysentery in demonstrating the parasite. If cysts are to be searched for, the use of the iodine-stained preparations of the stools, combined with culture methods, if the microscopical examination is negative, should be employed. Concentration methods should also be used in examining the feces for cysts.

St. John (1926) was the first to call attention to the value of culture methods combined with microscopical examination in the diagnosis of *Endamoeba histolytica* and his work was confirmed in 1927 by Craig and St. John and has been repeatedly confirmed since that time. Recent experience in the examination of food handlers in Chicago has again demonstrated the value of culture methods in the diagnosis of this parasite and it is believed that in every case where direct microscopical examination results negatively culture methods should be employed. In cases in which the feces are found to be negative upon repeated examinations, the proctoscope may possibly aid in diagnosis.

The *complement-fixation test* for amebiasis devised by myself (1927-1928) has proven of value in the diagnosis of this infection and appears to be practically specific with the exception that a considerable number of cases of chronic colitis give a positive reaction for some unknown reason, according to Kiefer (1932). This test is a very technical one and the antigen used is very difficult of preparation so that it has not been employed on a large scale except by a few investigators. At the present time, owing to technical difficulties, largely inherent in the preparation of the antigen, and because we are yet ignorant of the percentage of cases of non-amebic colitis which may react positively, *this test cannot be used alone* in the diagnosis of amebic infection and should not be so used in surveys of food handlers, as has been suggested by some physicians. It has been my experience that, in practically every case giving a positive complement fixation test, it has also been possible to demonstrate *Endamoeba histolytica* in the feces of the patient and that a careful examination of the feces would have led to a correct diagnosis without the aid of the complement fixation test. Certainly, at the present time, we have no method of diagnosis superior to the actual demonstration of *Endamoeba histolytica* in the stools of the suspected individual.

Space forbids the discussion of the diagnostic aid that is furnished by a microscopical study of the cellular exudates in amebic dysentery and bacillary dysentery, an aid

that has been stressed by Callender (1925) and Haughwaut and Callender (1925) in recent years. The presence of Charcot-Leyden crystals and the absence of pus cells and macrophages in the amebic exudate, together with many cells showing pyknotic nuclei, differentiate the amebic exudate from that of bacillary dysentery in which large numbers of pus cells and macrophage cells of endothelial origin occur.

Here, again, one must remember that bacillary dysentery may coexist with amebic dysentery, or occur in a carrier of *Endamoeba histolytica;* that the finding of this ameba in the stools does not negate a possible bacillary infection; and that the character of the exudate may be changed owing to the coexistence of the two infections.

The PROPHYLAXIS of infection with *Endamoeba histolytica* depends entirely upon the prevention of the contamination of food and drink with the cysts of the parasite. A properly guarded and impounded water supply; the proper disposal of sewage; the protection of food from flies; and, most important of all, in well sanitated districts, the examination and proper treatment of food handlers in public eating places are the methods of prophylaxis which are indicated. In regions where there is no filtered water supply and the inhabitants have to obtain their water from wells, springs, and other similar sources, it is well to remember that such water can be rendered safe only by boiling, as no chemical has been found that will kill the cysts of *Endamoeba histolytica* in amounts which may be safely added to water. Chlorine, so useful in the sterilization of water for pathogenic bacteria, is absolutely useless, as it requires practically 100 times as much chlorine to kill the cysts of this parasite when added to water containing them as is used in ordinary water purification, and such an amount of chlorine would render the water unfit for domestic consumption.

The routine examination of food handlers and their proper treatment is a most important prophylactic measure but, like so many prophylactic measures, involves economic questions which must be considered and upon the solution of which must depend the success of the measure. Ideally, if all food handlers in public eating places could be examined at intervals of six months, those found infected removed from their occupation, treated, and not allowed to resume their work until their amebae had been eliminated, the incidence of amebiasis and amebic dysentery would be very greatly reduced, but it is obvious that this is an ideal impossible of attainment and economically very costly. The loss of time and money by the infected individual, the loss to his employer, the cost of treatment and of the necessary examinations, all have to be considered in an estimation of the practicability of the routine examination of public food handlers.

Just how much can be done in the way of examinations of food handlers will always be a local question but I believe, despite the expense involved and the inconvenience resulting from such examinations, as much should be done as is possible and that the good accomplished will more than offset the many difficulties as will be encountered in such a program.

It is certainly most essential that the public be protected, as far as possible, from this infection and as much should be done in the examination of food handlers as can be accomplished with the means at hand. A campaign of education regarding the prevalence of amebiasis and the measures that can be used in every household to guard against it, would be productive of much good, while the examination of food handlers in large hotels and restaurants, and their treatment if found infected certainly will result in greatly decreasing the incidence of the infection in any locality.

Just a few remarks regarding the TREATMENT OF AMEBIASIS and amebic dysentery. At the present time we are fortunate in possessing several drugs that are practically specific in the treatment of infection with *Endamoeba histolytica,* both in carriers and in those suffering from symptoms of the infection, including amebic dysentery.

Those which have been found most useful in curing infections with this parasite are chiniofon, vioform, carbarsone, treparsol, and acetarsone. Emetine is most valuable in the control of the dysenteric symptoms in amebic dysentery. For the treatment of carriers, either with or without symptoms, emetine should never be used, as this drug cures a very small percentage of infections. In 118 cases of amebic dysentery observed by myself, in which from one to two 12-grain courses of emetine hydrochloride were administered subcutaneously, no less than 85 per cent showed cysts in the stools within two to four weeks after completing treatment, thus proving that this drug is far inferior to the others mentioned in actually curing the infections.

It is most unfortunate that many of our text-books still state that emetine is a specific in amebic dysentery and that the profession, generally, still believes that this drug is the one that should be employed for curative purposes in amebiasis and amebic dysentery. As stated, *it should never be used except to control the symptoms of dysentery* and then the dose should never exceed one grain daily for, at most, 12 days. It is good treatment in amebic dysentery to administer emetine hydrochloride to control the acute symptoms and then to give a course of one of the other drugs which has been mentioned. Of these, chiniofon has proven very successful in my hands but carbarsone, treparsol, and vioform have all been demonstrated to be most valuable in curing infections with *Endamoeba histolytica.* Acetarsone I no longer use as it has proven to be too toxic while both carbarsone and treparsol are as efficient and less toxic. Any one of these drugs, if properly administered, will cure the vast majority of infections with this parasite, the only exceptions being long continued cases of chronic amebic dysentery, in which the prognosis as to cure is exceedingly poor.

In conclusion, may I again call attention to the importance of infection with *Endamoeba histolytica,* or amebiasis, to the health of the people of the United States. Amebiasis is a real public health problem and one that demands the most careful study, and it is greatly to the credit of the Department of Health of this great city and to the members of the local medical profession that its importance has been recognized and measures have been taken to control this infection.

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AMEBIC DYSENTERY IN CHICAGO

By

HERMAN N. BUNDESEN, M.D., Sc.D.

President of the Board of Health

CHICAGO, ILLINOIS

UNTIL August, 1933, one or two cases of amebic dysentery were reported each month in Chicago. This is the usual level, and was no cause for alarm. On August 15, however, two cases were reported, one each by a hospital at which the patients were being treated. These cases were investigated because it was felt that there might be some significance to the reporting of two cases on one day. It was found that both patients had eaten at a certain hotel in Chicago. An investigation was immediately ordered, and a staff sent to the hotel for the purpose.

Control measures were established immediately. These included:

1. The prompt isolation and treatment of all cases and carriers.
2. Stringent sanitation in toilets in regard to washing the hands.
3. The prohibition of food handlers with stools positive for *Endameba histolytica* from returning to their work after treatment until they had had three negative specimens of feces taken at intervals of one week, and a final negative following a laxative, one month later.

Of 364 food handlers from the hotel who were examined up to September 1, twenty-six were found who had *Endameba histolytica* in the stools; of these, fifteen had some slight symptoms, such as diarrhea. A preliminary report of this was made, October 9, by Fred O. Tonney, Gerald L. Hoeft, and Bertha Kaplan Spector before the Laboratory Section of the American Public Health Association in Indianapolis.

As soon as a person was found to be harboring the ameba within his intestinal tract, he was excluded from the hotel.

Later, on October 25, a second examination was made of all the food handlers of the hotels, as well as of the non-food handlers. On the second examination, feces were obtained from all of the food handlers previously examined except the twenty-six who had been excluded.

It was found that 60 had *Endameba histolytica* in the stools who were negative on the first examination; 498 non-food handlers were examined, and 100 were found to have *Endameba histolytica* in the stools. Three additional surveys of the food handlers in this hotel were made starting in November, with a decreasing percentage of positive cases being found on each examination. However, on the fifth survey, there were still about eight per cent. of those examined who were found to be carriers of the *Endameba histolytica*.

Like other infections with protozoa, those with endameba produce a variety of symptoms. The disorder may be fatal in a short time; it may be severe for a long or a short period. The disorder may become chronic, with alternating periods of diarrhea and constipation. It may be mild and cause little discomfort. In addition, the incubation period of the disease seems to vary from nine to ninety-five days.

The great majority of the persons patronizing the hotels were not residents of Chicago. Frequently, those infected had returned to their homes in some distant city before symptoms became apparent. Consequently, when the second survey showed a greater percentage of carriers from the food handlers than the three to five per cent. which is normally expected, it was decided to send a questionnaire to the out-of-town guests of the hotel chiefly concerned.

After the second survey, started on October 25, we felt that the probable date of the outbreak seemed to be about July 1, 1933. But questionnaires were sent to individuals who had registered several months before that date. Of 22,000 questionnaires sent out, approximately 200 were returned because of the wrong address. Up to November 14, approximately 3,490 replies had been received.

In the questionnaire, information was requested as to any illness occurring during or after a visit to Chicago. On 3,490 questionnaires, 180 reported illnesses. Of these, 69 were positively diagnosed as amebic dysentery, 23 were reported as suspected of having amebic dysentery, and 88 were reported as having disorders other than amebic dysentery. Among the disorders listed were ulcerative colitis, mucous colitis, and appendicitis. Many of the persons suspected of having an amebic infection had bloody stools and diarrhea. All of the individuals had outbreaks of diarrhea after they had eaten at the hotels concerned. It was not until these questionnaires were returned that there was sufficient evidence at hand to make it certain that a very wide outbreak of amebic dysentery had occurred.

From the first day that we were notified of the existence of a case of amebic dysentery, and every day thereafter, as soon as a case was reported to us, we immediately notified the State Director of Health at Springfield, Illinois, and he, in turn, made a report of those cases to the United States Public Health Service by telegraph each Monday. After thoroughly investigating the situation here in Chicago, Dr. Roscoe R. Spencer, of the United States Public Health service, issued the following statement:

"Everything humanly possible has been done to control the outbreak. There is certainly no need for any general alarm. Dr. Bundesen and the Board of Health are to be congratulated on the promptness, aggressiveness, and thoroughness with which the situation has been handled."

From January 22 to January 26, 1934, a committee assembled in Chicago to make a study of the outbreak of amebic dysentery which occurred, and also to inspect at first hand the premises concerned. It was brought out that water and sewer systems in older hotels in Chicago and throughout the country in old buildings are antiquated, and a potential source of danger. Under special circumstances, such as overloading, they may produce extensive pollution of the water supply.

Up to February 2, 1934, 774 cases of amebic dysentery were reported from 213 cities, with 42 deaths, the probable origin being traced to the Chicago outbreak. We have discovered 1,130 carriers. Our investigations are being continued in the hope that we can secure even more definite evidence to prove the findings of this committee.

Between 1921 and 1927, there were 33 deaths from amebic dysentery in Chicago. Outbreaks of amebic dysentery are, in many cases, undoubtedly the result of infection transmitted by carriers of *Endameba histolytica* who are engaged in food handling. For this reason, all food handlers should be carefully examined and reëxamined, and specimens of feces studied for the presence of the parasite.

In all cases of diarrhea or chronic intestinal disorders, a careful search should be made in stools for the presence of *Endameba histolytica*. In many respects, amebic dysentery is a real hazard and demands the attention of health officers.

"CERTAIN ATYPICAL TYPES OF AMEBIASIS"*

By

PHILIP W. BROWN, M.D.†

ROCHESTER, MINNESOTA

THE epidemic of amebic dysentery confronting the medical profession has served to drive home a fact which has been well known for more than twenty years. Sistrunk's first report, in 1911, of amebiasis in the Northwest has been followed by numerous other articles. A previous report[2] and that by Craig suggest that the incidence of amebiasis in the United States is approximately 5 per cent. Although only a few of those infected may have any subjective symptoms, yet it should be emphasized again that all these people constitute a potential menace to themselves as well as to the community. Direct transference of cysts to food, either by food handlers or by flies, is definitely established; the infection of a large number of individuals within a certain time, however, suggests the contamination of a water supply, such as has been so well illustrated in epidemics of typhoid fever. Infection of vegetables, such as celery and lettuce, by irrigating fields with water into which sewage has been poured is a most unpleasant thought and may be a possibility, but no very striking proof of this mode of transmission has been offered.

The important phase of the present problem is well expressed by an editorial in *"Annals of Internal Medicine"*: "It is not in connection with the outspoken clinical manifestations of amebiasis that the main problem exists; it is rather with the far greater number of instances in which amebiasis is present without producing any characteristic symptoms." Already there has been sufficient evidence[5] to demonstrate that the parasite may produce marked lesions, particular in the cecum, without appreciable clinical signs. Although it is not proved that all infected individuals have pathologic lesions, yet the fact that lesions do occur and that the *Endameba histolytica* is a tissue parasite should lead us to think only of "latent" and "active" cases, discarding entirely the term "carrier." Craig long has insisted that the proper conception of amebiasis is that *Endameba histolytica* is a tissue parasite and must produce some injury to the bowel, however minute the lesions may be; hence, the case is latent or active depending on the extent and severity of the lesions as well as on the resistance of the individual. Although, in the majority of cases, an equilibrium is maintained between destruction by the parasite and repair by the host, yet even in the sturdiest individuals a grave menace exists, not only to them but also to others for whom they are a constant focus of infection.

The public health aspect of the condition as well as the manifestations of acute, amebic colitis and hepatic abscess have been dealt with in various other articles. I propose to deal chiefly with some atypical varieties of active amebiasis and with the dramatic symptoms that may develop in latent cases. It may be assumed that diarrhea will now more than previously cause search to be made for *Endameba histolytica*, but can one obtain any clues which will serve to diagnose amebiasis in the atypical and latent manifestations of the disease?

Examination of the stool for parasites is advisable in all peculiar cases; but immediately doubt may arise as to the competency of the examiner, because it is not always possible, even for the expert, immediately to be successful in his search unless time permits repeated stool examinations, supplemented perhaps by cultural studies. Sigmoidoscopic examination is strongly suggestive if it discloses amebic ulcers. Likewise, though less diagnostic, the opaque enema may reveal evidences of irritability or thickening of the bowels, especially in the cecal region. It is to be hoped that Craig's or some other similar type of complement-fixation test may become generally available; it has not been practicable yet because of the great difficulties involved in producing sufficient quantities of antigen.

At this Clinic and elsewhere, I have encountered unusual problems which are illustrated by the following cases. They are examples of what is particularly likely to be encountered in a consulting practice in gastro-enterology.

> CASE 1.—A man, aged 44, requested an opinion as to advisability of nasal surgery. He made no other complaint except that he suffered from fatigue, which he attributed to overwork. Shortly before his dismissal, he was seized with a severe chill and fever. He was promptly hospitalized. In forty-eight hours, definite signs of bronchopneumonia of the right lung were elicited. A pleural effusion developed and aspiration was necessary. Hemolytic streptococci were identified in cultures of this effusion. During the tenth night of the illness, a clotted stool with bright red blood was passed and was followed within a short time by two more, and by larger passages of red blood. Prior to and following this, there were no abdominal symptoms. Sigmoidoscopic examination gave negative results. An examination of material obtained by rectal tube disclosed no parasites. The further course was progressively downhill, in spite of repeated blood transfusions, oxygen therapy, and so forth. At necropsy, ulcerated, elevated plaques were found at the head of the cecum and, further on in the cecal area, were many shallow ulcerations (fig. 1). Four small, punched-out ulcers were found in the rectum. Microscopic examination of smears from the cecal ulcers revealed *Endameba histolytica*.

In amebiasis, massive hemorrhage from the colon is rare, although I have seen it in both chronic ulcerative colitis and in rectal carcinoma. Bloody discharges are common, however, and may produce marked anemia. The absence of any intestinal symptoms, even after the hemorrhage, is striking. In the case cited, a hemolytic streptococcal pneumonia with empyema offers a grave prognosis. The hemorrhage greatly diminished resistance and vitality. I consider this as a latent case of amebiasis in which resistance had been so lowered by a severe form of pneumonia that the amebas began to thrive. This is further confirmed by the presence of rectal ulcers found at necropsy, but which were not present six days previously.

How can one suspect such a complication? It is scarcely feasible to order a series of daily examinations of the stool of every patient who is ill. In this case, after the hemorrhages, no stools were passed that could be examined. Also, I feel that the outcome was all but inevitable because of the pneumonia. However, if one is confronted with the grave problem of massive, red bloody passages, bear in mind the possibility of bleeding amebic ulcers and promptly institute treatment with emetine. This condition constitutes a grave emergency and there is no time for special studies. Such a course of emetine treatment may not be a scientific procedure, but it may be life-saving. Surgical intervention almost surely would be fatal. Exploring the colon for acute perforation or bleeding points is a most serious undertaking and, if the condition is amebic ulceration, the result of surgery has been illustrated by the events of past months.

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†Division of Medicine, The Mayo Clinic, Rochester, Minnesota.

2. Brown, P. W.: Endamebiasis as seen at The Mayo Clinic. *Proc. Staff Meetings of Mayo Clinic*, 7:43-47 (Jan. 27) 1932.

5. Dock, George; Musgrave, W. E., Bartlett, C., and James, W. M.: Quoted by Craig.



Fig. 1. Acute and chronic amebic ulcerations of cecum.

CASE 2.—Less dramatic is the case of a young woman who complained of moderately severe, lower right abdominal distress. Leukocytes were found to number 16,000 per cubic millimeter of blood. There was no fever. A preoperative diagnosis of subacute appendicitis was made. At operation, the appendix seemed normal but the walls of the colon were thickened and plaque-like due to a diffuse inflammatory process. Regional lymph-nodes were enlarged, and a careful biopsy of one revealed an inflammatory condition. The abdomen was closed. Later investigation disclosed that the patient had had a few days of abdominal discomfort associated with mild diarrhea, two and a half months previously. Since then, vague distress slowly had increased to the point where the patient had obtained a leukocyte count and reported for examination. Examination of the stool revealed *Endameba histolytica*. The institution of anti-amebic treatment gave an apparently satisfactory result, as proved by recent negative tests.

This is another of the peculiar types of amebiasis which may arise. Very careful questioning led one to suspect an amebic condition, yet the few days of diarrhea more than two months prior to admission was the only definite sign. The patient considered that the few days of gradually increasing discomfort was independent of any antecedent condition, and in a young individual with this complaint, the diagnosis of appendicitis was logical. In retrospect, there was little doubt of an inflammatory condition, but as the process apparently was not progressing from bad to worse, the thought arose that strict observation and suitable studies could be started, while being prepared to operate at any time if further developments pointed more and more sharply toward appendicitis. The death rate from appendicitis has been mounting in the last few years and so, again, one must be alert not to urge, nor yet unduly to delay, surgical intervention. In such a case, exceedingly close coöperation between internist and surgeon is imperative.

CASE 3.—A man, aged 54, stated that for six weeks, he had suffered from gradually increasing abdominal cramps and colicky pains associated with constipation. There was much audible rumbling in the abdomen. Relief was obtained from movement of the bowels. No blood had been seen in the stools. A proctoscopic examination had been made elsewhere and was reported as having revealed rectal inflammation. The abdomen was somewhat distended; an irregular mass was felt in the lower right quadrant, but there was no pain. The blood count was normal. *Proctoscopic examination* revealed several large, irregular areas of ulceration throughout the rectum and sigmoid. An opaque enema revealed a filling-defect involving the cecum in the region of the ileocecal valve (fig. 2). There was no ileal involvement. Examinations of the stool on two successive days disclosed no parasites. In view of the patient's age and the presence of a palpable mass and subacute obstruction the question arose as to whether this might be a tumefactive cecal mass, due perhaps to *Endameba histolytica*, or whether there were two conditions, cecal carcinoma and amebiasis. The suspicion of amebiasis was scarcely more than a "hunch", as negative stools and peculiar rectal ulcers were not diagnostic. The patient was hospitalized. Residue-free diet and anti-amebic treatment were instituted. Subjective improvement occurred within four days and, after ten days, the rectal ulcers had disappeared and no abdominal mass was felt. An opaque enema revealed marked decrease in the cecal filling-defect and, three weeks later, the colon was practically normal.

Tumefactive masses due to *Endameba histolytica* are not common. They are most likely to occur in the cecal or sigmoidal regions. To the well-trained roentgenologist, the lesion of the cecum in this case is not typical of carcinoma, although error in interpretation readily might occur. In the presence of cecal mass and obstruction, and in doubt as to the roentgenologic interpretation, one might advise surgery. It is regrettable that *Endameba histolytica* was not identified in this case, so that a positive diagnosis could have been established. However, a suspicious mind and the atypical combination of roentgenologic and procto-

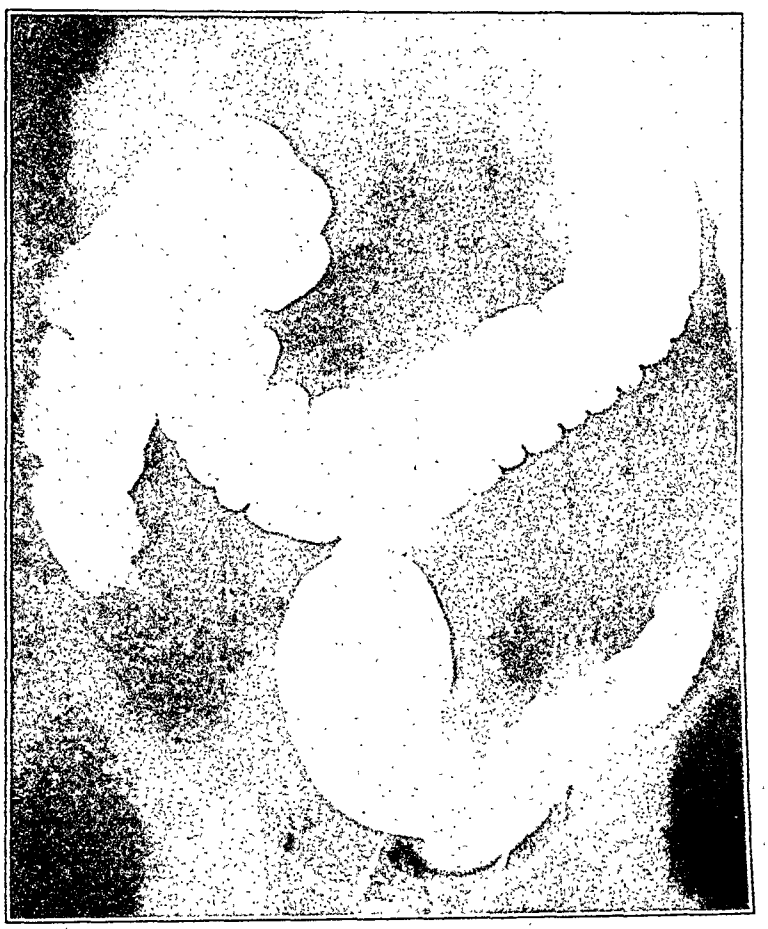


Fig. 2. Amebic tumefactive cecal mass; the conical cecum and normal terminal portion of ileum may be noted.

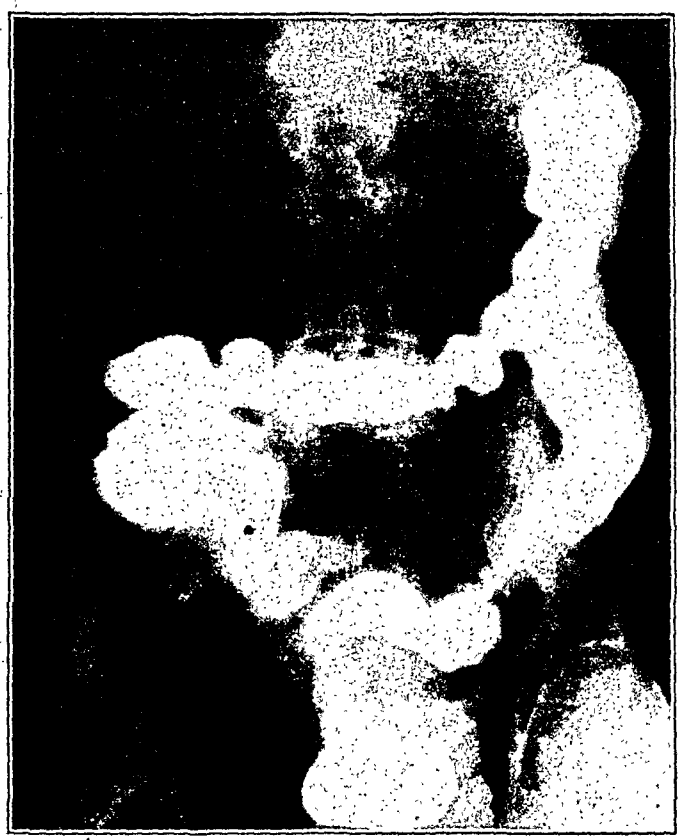


Fig. 3. Diffuse ulcerative colitis due to amebiasis. Right hemicolectomy done previously accounts for failure to show cecum.

scopic findings did suggest observation and anti-amebic treatment. The response to the treatment seems strongly enough presumptive evidence to consider this case probably as amebiasis.

CASE 4.—A man, aged 48, complained of bloody diarrhea of two years' duration. The bowels had moved twelve to twenty times in the course of twenty-four hours. Weakness and anemia had become severe. Previous examinations of the stool had given negative results, but proctoscopic and roentgenologic signs of chronic ulcerative colitis had been present. All manner of diets, transfusions, winters in California and Florida, and various nonspecific measures had proved unavailing. The patient had been taking 60 drops of tincture of opium daily for twenty-one months.

On examination, the patient was seen to be thin, pale, and very weak. There was marked hemoglobinemia (45 per cent by the Dare method). Proctoscopic examination revealed granular, easily-bleeding mucosa and contraction of the lumen of the bowel to 50 per cent of its normal diameter. Cultures for Bargen's diplococcus were taken and later reported negative. An opaque enema (fig. 3) disclosed abnormalities in the entire colon, such as may occur in chronic ulcerative colitis. It probably was fortuitous but, in the first examination of the stool, the specimen was almost alive with *Endameba histolytica*. Within forty-eight hours after instituting anti-amebic treatment, the patient reported that he felt better and the bowels were almost normal for the first time in two years. Examinations months later gave negative results (fig. 4). He has had no recurrence of dysentery.

Although this is the bloody diarrhea type, yet it had proved resistant to all previous treatment because the proctoscopic and roentgenologic findings characteristic of ulcerative colitis had been misleading. On questioning the patient, he informed me that many examinations of his stool had been made by hospital internes. I do not feel that the responsibility for such examinations should be placed in the hands of internes or of ordinary laboratory workers; it is no reflection on their ability, but, if one is to rely on stool reports, the examination must be made by those competent to do so. Years ago, Logan urged not only routine examination of the stools for parasites in chronic ulcerative colitis cases, but also suggested that a therapeutic course of emetine was always a wise procedure. Certainly the emetine will do no harm and occasionally may, as the Chinese say, "save one's face."

CASE 5.—Proof that this patient had been infected with *Endameba histolytica* was not confirmed by the identification of the parasite (as in case 3). The clinical response to anti-amebic treatment is so striking that I feel justified in considering this as another peculiar type of latent amebiasis. I am not familiar with any morbid condition, except amebiasis, which will be so greatly improved by emetine within forty-eight to sixty hours.

This patient, a woman, had suffered vague abdominal distress for three weeks when pain in the lower part of the abdomen had become severe. Her bowels had moved normally once to twice daily. Fever developed and she had several chills. The only significant findings were the temperature of 103°F., leukocytosis of over 20,000, and evidence, from bimanual examination, of marked pelvic inflammation, especially on the right side. For seventy days, the course was stormy, the temperature high, and there was persistent leukocytosis. At no time did it seem advisable to attempt surgical intervention. In the seventh week, a bloody, foul, rectal discharge developed, as if an abscess had ruptured spontaneously into the rectum. This gave slight relief from pain, but otherwise there was no particular improvement as usually occurs after evacuation of an abscess due to a ruptured appendix or to tubo-ovarian infection. After a few more days, the suggestion of amebic abscess was made because the patient had been in Chicago during the late summer. Examinations of her stool did not reveal any parasites; however, a therapeutic course of emetine produced a prompt drop in the temperature, the symptoms gradually abated, and, for the first time in weeks, the patient showed definite improvement, which has been maintained. The discharge ceased, and, with continuation of anti-amebic therapy, it is hoped that there will be no further trouble. The patient would not permit a proctoscopic examination to be made which might have revealed ulcers. At no time would it have been feasible to obtain a barium enema owing to the acuteness of the disease.

I am certain that criticism properly may be offered that this case should not be considered as one of amebiasis, but, as already stated, the clinical response was so striking and



Fig. 4. Condition of colon after anti-amebic treatment.

because it does not occur in any other condition with which I am familiar, that clinically one must consider it as a case of amebiasis. Quite likely there were ulcerations in the cecal area which had perforated and produced an amebic abscess in the pelvis.

The problem of latent and atypical varieties of amebiasis constitutes a grave responsibility for both medical and surgical men. The institution of anti-amebic treatment without establishing a positive diagnosis is to be deprecated. Facilities for adequate and reliable examinations of stools must be obtained. The supplements to investigation of intestinal diseases should be utilized more and more; namely, proctoscopic studies and studies of the colon by means of opaque enemas. However, grave emergencies may arise or conditions may exist that preclude special studies, so that I think that the final responsibility rests on the attending physician to maintain a low "threshold of suspicion" for the possibility of amebiasis and to consider administration of a therapeutic course of emetine.

TREATMENT

As no present drugs, or any combination of drugs, provide the best method for the treatment of amebiasis, an extraordinary number of therapeutic suggestions have been offered, but I will not attempt to discuss them.

The regimen that I have carried out for seven years has been as effective as any with which I am familiar. Briefly, it is based on the fact that emetine controls the acute manifestations of the disease better than any other known drug. As emetine or any ipecac derivative fails to produce cures in about two-thirds of the cases, an arsenical drug is combined in the regimen, as arsenic seems more effective in eradicating the parasite. My experience with *yatren* (sometimes known as anayodin, quinoxl or chinofon) or with *vioform* is that neither is generally as effective as the emetine-arsenic regimen, although I have found them valuable and occasionally effective aids in some cases. Medicated colonic irrigations are of so little if any value that I do not use them.

A therapeutic course of emetine may be defined as ⅔ to 1 grain (0.043 to 0.065 gm.) of emetine hydrochloride administered subcutaneously twice daily for three days.

A "course" of anti-amebic treatment is as follows:

1. Emetine hydrochloride, ⅔ to 1 grain, administered subcutaneously twice daily for three days and repeated after a week's interval.

2. *Treparsol*, 1 tablet (0.25 gm.) administered orally with each of the three meals for four days, and repeated in two more such courses, allowing a ten-day rest period between each course.

As both emetine and arsenic (treparsol) are poisons and may produce either early or late evidences of intoxication, these drugs must not be used except under close supervision. Undoubtedly, the chief factor in intoxication is that of sensitivity of the individual, but this factor can seldom be known in advance. It is in cases in which emetine or arsenic has been administered when patients are hypersensitive to them, or in recurrent cases, that I resort to yatren or to vioform. Both these drugs are administered orally; yatren, 3 gm. daily for ten days and repeated after a week's interval; vioform, 0.75 gm. daily in the same manner. Yatren tends to produce intestinal irritation and the daily dose may need to be decreased, thereby prolonging each course.

As previously stated,[3] I think that the chief difficulty in obtaining good results is the failure to persist in adequate and properly timed treatment. Following the course of treatment, stools should be examined on three successive days; if the results are negative, this should be repeated at the end of a month and, again, two or three months later.

CONCLUSIONS

1. The term "carrier" should be discarded and the term "latent case" employed.

2. Latent cases of amebiasis may produce peculiar and even grave complications in the course of any debilitating condition, or they may give rise to a *bizarre* symptom complex with none of the usual manifestations of dysentery.

3. Atypical types of amebiasis may be confused with true chronic ulcerative colitis or with carcinoma.

4. A program of treatment and reasons therefor have briefly been stated.

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MIGRAINE, AN ALLERGIC PHENOMENON*

By

ALBERT F. R. ANDRESEN, M.D., F.A.C.P.,
BROOKLYN, NEW YORK

THE term "migraine" has long been used loosely to designate all kinds of headaches and has in recent years been applied even to attacks of abdominal symptoms alone, but similar to those often accompanied by headache. It must be recognized that migraine is not a disease, but that the word is used to describe a syndrome. In order to form a basis for study, there should not be a tendency to make the word embrace an ever-increasing group of symptoms, but to limit it to designate a well-defined symptom-complex. "Migraine" should be confined to a condition associated with periodic attacks of headache and vomiting, the former usually unilateral in type, often preceded by an *aura*, and occasionally accompanied or followed by abdominal pains, diarrhea or polyuria, not explainable on the basis of an actual pathological lesion, and therefore sometimes called "idiopathic migraine".

The most exhaustive review of the literature of migraine, and one of the most complete studies of a disease or symptom made in recent years, is that made by Henry Alsop Riley, and published November, 1932, in the Bulletin of the Neurological Institute of New York. This review shows what a diversity of opinion has been held respecting all phases of migraine, not only in regard to what constitutes migraine, but also in regard to its etiology, its pathology and its treatment. However, the various types of migraine described in this review would not all fit the description of the syndrome as outlined above. "Abdominal" migraine, as mentioned before, would be ruled out, "ophthalmic" or "ophthalmoplegic migraine", if due to definite eye or brain pathology, would not be included, and "sinus migraine", with its definite pathologic basis, would not belong in this category.

Migraine is a common condition. It has been estimated that 7 per cent of the total population is subject to attacks of this syndrome and it has been shown to occur more frequently among those of a high degree of intelligence. Its hereditary basis long has been recognized, various members of a family often taking turns at being disabled by its manifestations. The familiar "bilious attacks", so commonly described, and usually attributed to a large variety of conditions, are in a large proportion of cases typical migraine attacks. In a series of 3,170 private patients applying to us for relief of gastrointestinal complaints, we found that 150, or 4 per cent, had the typical symptoms of migraine, and these patients have formed the basis of this study. Only 15 of these patients (10 per cent) had symptoms of migraine alone, the remainder mentioning it merely as one of the symptoms occurring in addition to other, usually more serious, gastrointestinal complaints. A partial list of these diseases and the percentage of their occurrence in this group of 150 patients, is shown in Table 1.

TABLE 1. Coincident Lesions Found in a Study of 150 Migraine Patients.

Other Diseases Present	*Number*	*Per Cent*
Gastro-duodenal ulcer	27	18
Gastro-duodenitis	38	25
Biliary Tract Diseases	21	14
Chronic Appendicitis	41	27
Chronic Colitis	25	17
Other Colonic Conditions	15	10
Cardiovascular Diseases	14	9
Endocrine Disturbances	13	8

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ETIOLOGY

In an effort to find a cause for migraine all sorts of theories have been advanced. The term "bilious attack" having so often been used to describe the condition, probably due to the frequent vomiting of bile, a biliary origin has been sought, and many patients have been subjected to futile surgical procedures, with the biliary tract as the initial point of attack. When this region was found normal at operation, the necessity for doing something usually resulted in an appendicectomy or some other operation being performed, the migraine attacks subsequently continuing as before. In my series of 150 patients, operations had previously been performed in 53, or 35 per cent, the nature of the principal operations being shown in Table 2.

TABLE 2. Previous Operations in 150 Private Patients With Migraine.

Previous Operations	*Number*	*Per Cent*
Appendicectomy	25	16.6
Cholecystectomy	5	3.3
For Peptic Ulcer	3	2.0
Pelvic Operations	11	7.3
Other Operations	9	6.0
Total	53	35.2

Local conditions, such as refractive errors or eye pathology, nasopharyngeal or oral lesions, or facial or cervical abscesses, tumors or skin conditions, where producing headaches from peripheral nerve irritation, do not usually cause the other coincident symptoms of typical migraine, and even when they do, such cases would not be included in the definition of migraine on which we have decided. However, focal infection plays an important rôle in the etiology, as shown by the fact that often the mere removal of foci has resulted in a cessation of the attacks for long periods of time, probably due to a general beneficial effect on the patient's condition. In our series of 150 patients, 141, or 94 per cent, had definite foci of infection, but in only 26, or 18 per cent, did we feel that their presence was the predominant factor in the production of symptoms.

The *age* of onset of symptoms constitutes an interesting study. While the average age of the 150 patients consulting us, more particularly in regard to their gastrointestinal symptoms, was 39 years, their histories disclosed that migraine symptoms had developed in earlier life. Eighty-two had developed migraine symptoms before the age of 20 years, yet only 10 had had symptoms before the age of 10, so that 72 patients, or 48 per cent of this series, placed the onset of symptoms definitely in the period of puberty. The other statistics in regard to age are shown in Table 3. *Sex* does not play an important part in the etiology. Although 90 of our patients were women (60 per cent), we believe that in any series of 150 patients consulting a clinician for gastrointestinal complaints at the end of the fourth decade of life, more than 60 per cent would be women. Only 60 per cent of the patients were married.

TABLE 3. Age Incidence in 150 Migraine Patients.

Average age on applying for treatment	39 years	
Average age of onset of migraine	16.8 years	
	Number	*Per Cent*
Age of onset under 10 years	10	7
10 to 20 years	72	48
20 to 30 years	37	25
30 to 40 years	22	14
40 or over	9	6

The relation of migraine to the *endocrine system* has been pointed out. The frequent occurrence of attacks at the menstrual epoch and called "menstrual migraine", has indicated its ovarian origin. Twenty-five of our 150 patients, or 17 per cent, had this type of occurrence. The frequent onset of symptoms at puberty and their disappearance after the menopause has also indicated a gonadal relationship. The relation to the pituitary has been pointed out, and an effort has been made to prove by Roentgen-ray studies of the *sella turcica* that there is a diminished amount of room for expansion of the pituitary in migraine cases, and that such temporary expansion is the mechanical factor causing the attack. It, however, has been shown that in known pituitary tumors typical migraine is not produced, and that even marked deformities of the *sella* may produce no symptoms at all. On the other hand the benefit derived at times from the use of pituitary extract in the treatment of migraine attacks, indicates that at least a functional disturbance of this gland may be a factor. The frequently sudden cessation of an attack following the administration of epinephrin or ephedrine suggests an adrenal etiology, and with a dimunition in blood calcium content during an attack, the effect of the use of parathyroid extract and calcium in aborting and even preventing migraine attacks, seems to be a further proof of an endocrine imbalance.

The *hereditary or familial factor* in migraine is well known. Whereas in only 28 of our 150 patients (19 per cent), was there a definite family history of migraine attacks, the history of other hereditary conditions, mostly allergic in origin, was much larger, although, unfortunately not always put down in the records. In a typical case of a patient who himself had only skin and gastrointestinal allergic manifestations, there was a history of asthma in the maternal grandmother, migraine in both parents and in the paternal grandmother and migraine in two of his three children, the other child having diarrheal attacks explainable on a dietary basis.

Dietary indiscretions as a cause of migraine attacks have been recognized for so long and the statements by patients that definite foods were known to produce the symptoms have been so frequent, that food allergy as a cause of migraine should long ago have been suspected. As a matter of fact, it is nearly twenty years since the writer first recognized that specific food-sensitization was an important etiologic factor in this condition, and since that time he has always considered migraine an interesting but not at all disturbing complication to treat. In our series of 150 patients, 77, or 58 per cent, were shown to have attacks as a result of food sensitivity. In 1925, in an article on food allergy[1], we mentioned migraine with asthma and hay fever as an example of an allergic manifestation and were surprised that it occasioned comment. Our study on migraine followed in 1931[2]. Meanwhile Ball[3], Vaughan[4], Balyeat[5], Rowe[6], and several foreign authors had made excellent contributions to the literature of the subject. Probably the most authoritative exposition has been presented by Foster Kennedy[7] who, after quoting the literature supporting the allergic theory, explains the occurrence of symptoms on the basis of a localized intracranial edema similar to the edema seen in the skin in urticaria or angioneurotic edema.

Allergy can be used to explain a number of apparent discrepancies in regard to migraine. Yet when one realizes how little is known about allergy itself, he realizes that such an explanation only seems to explain. At first considered synonymous with "protein sensitization" and closely related to anaphylaxis, the word "allergy" has also been made to include sensitivity to non-protein drugs and chemical substances and even to physical agents such as heat, cold and electricity. While the resemblance between the problems of allergy and those of infection and immunity has been repeatedly pointed out, there is, as yet, no unanimity of opinion as to whether the allergic reaction corresponds to susceptibility to infection or to immunity. The intensive study of asthma and hay fever has disclosed that these allergic manifestations, while frequently caused by inhaled or ingested proteins, may also be caused by sensitization to bacterial proteins or to some of the factors produced at a point of active infection and absorption, such as an infected sinus or tooth. Thus we have an explanation of the probable relation between focal infection and migraine. In the case of menstrual migraine, a sensitization to ovarian hormone or to some of the other products elaborated during the process of menstruation, will explain this phenomenon. That a person may become sensitized to his own internal secretions is a possible explanation of the typical migraine attacks which sometimes follow great mental stress (anger, fear and grief), all probably associated with a sudden increase in adrenal secretion. However, the relation between the endocrine system and allergy in general has long been recognized, and the use of extracts of various endocrine glands, particularly the adrenal and the pituitary glands, has become a routine in the treatment of allergic manifestations.

PATHOLOGY

A characteristic of all allergic reactions is that the lesion produced is only temporary and that it usually disappears at death, so that at autopsy no lesions can be found, except where, as a result of long continued or repeated reactions certain changes have been produced. In other allergic conditions these may be quite marked, as, for instance, in asthma, where an emphysema is the result of the prolonged irritation, in eczema, where a thickened skin is produced and in colonic allergy ("colitis") where the bowel wall becomes fibrotic and stiffened . In general, the local allergic reaction can be described as due to irritation, the irritant being the substance to which the patient is sensitized. This irritant may come into direct external contact with the tissues affected or it may be carried to them by the blood. The irritation may result in skin or mucosal manifestations, such as rashes, wheals, edematous areas, purpuric spots, necrotic areas or hemorrhages, or in neuromuscular manifestations, such as the spasms of asthma and the colic of gastrointestinal allergy. Excretion of the *allergen* also may cause local irritation, such conditions as polyuria, skin conditions and *pruritis ani* probably belonging to this type of reaction.

The *lesion* of migraine never has been demonstrated: autopsies in sufferers from migraine having failed to show any constant lesions. Kennedy, as mentioned above, has gone very thoroughly into the neurological phases of the situation and has stated that it would seem that a transient "edema of the cerebral meninges with especial pressure in the meningeal crevices produces the localized headache and the local cerebral symptoms of migraine".

SYMPTOMS

The most important symptoms of migraine consist of the occurrence, at varying intervals, of attacks of headaches and vomiting. Although unilateral headache, or *hemicrania*, often has been considered an essential symptom in making the diagnosis, other concurrent symptoms, even

1. Andresen, A. F. R.: Gastrointestinal Manifestations of Food Allergy. Medical Journal and Record, September 2, 1925.
2. Andresen, A. F. R.: Migraine. Medical Times and Long Island Med. Journ. Dec., 1931.
3. Bell, F. E.: Migraine, Its Treatment with Peptone and Its Familial Relation to Sensitization Diseases. Amer. Journ. Med. Sc. CLXXIII, 781, 788, 1927.
4. Vaughan, W. T.: Allergic Migraine. Journ. Amer. Med. Assoc. LXXXVIII, 1383, 1386, 1927.
5. Balyeat, R. M. & Brittain, F. L.: Allergic Migraine. Based on a study of 55 cases. Amer. Journ. Med. Sc. CLXXX, 212-221, 1930.
6. Rowe, A. H.: Allergic Toxemia and Migraine Due to Food Allergy: Report of Cases. California & West. Med. XXIII, 785-793, 1930.
7. Kennedy, Foster: Migraine: A Localized Intracranial Edema. International Clinics, Vol. III, 41st Series, 1931.

though linked with a general headache, when shown to be the result of the same allergic factor, really confirm the diagnosis. Hemicrania was present in 53 per cent of my cases (Table 4). The occurrence of an *aura*, usually consisting of a scintillating scotoma, or at times of other visual disturbances such as *hemianopsia* or transient blindness, is quite common, having been present in 39 per cent of our cases. Nausea occurred in 36 per cent of this series, and vomiting, either throughout the attack or at the end, occurred in 41 per cent. The vomitus, due to the fact that there was usually little or nothing in the stomach, consisted largely of bile, regurgitated into the stomach as a result of persistent retching. Abdominal pain was complained of during the attack in 21 per cent, and diarrhea occurred either during or at the end of the attack in 22 per cent of our cases, usually in those patients who did not vomit.

TABLE 4. Incidence of Typical Symptoms in a Study of 150 Patients with Migraine.

Symptoms	*Number*	*Per Cent*
Aura	58	39
Hemicrania	79	53
Nausea	55	36
Vomiting	62	41
Abdominal Pain	32	21
Diarrhea	33	22

The duration of the migrainous seizure may vary from a few hours to a number of days, and the interval between attacks from a few days to many months. Table 5 shows the statistics in regard to those details. Frequently the attacks end quite abruptly and there may be no symptoms afterward, or the patient may suffer from allergic reactions in other regions or the symptoms of his intercurrent disease.

TABLE 5. A Résumé of Some Findings in 150 Migraine Cases.

Conditions Found	*Number*	*Per Cent*
Neurotic Type	108	72
Chronic Constipation	65	43
Focal Infections	141	94
Gastric Anacidity	17	11
Hypertension (150 Syst. or over)	23	15
Hypotension (110 Syst. or under)	32	21

As mentioned before, nearly all (90 per cent) of the patients in the series under consideration came for the treatment of other symptoms, gastrointestinal in type, the lesions found being shown in Table 1. The symptoms of these gastrointestinal diseases were therefore also present and at times masked the migrainous attacks or were aggravated or even induced by them. It must be borne in mind, therefore, that the treatment of migraine may not be successful until all organic factors have been eliminated. It must also be emphasized that migraine patients are predominantly of the neurotic type. Table 6 shows that 72 per cent of our patients belonged in this category, and that, in addition, 43 per cent were habitually constipated.

TABLE 6. Duration of Migraine Attacks and Interval Between Attacks Shown in Study of 150 Migraine Patients.

Duration of Attacks	*Number*	*Per Cent*
12 Hours or less	48	32
1 or 2 Days	63	42
More than 2 days	20	13
Not noted	19	13
Interval Between Attacks		
1 Month or less	81	54
3 Months or more	27	18

Physical examination aside from disclosing, often, an individual of the neurotic or "spasmophilic" type of constitution, shows no characteristic findings. Focal infections, however, were noted in 94 per cent of our patients. Blood-pressure findings were not of special significance, the proportion of patients showing variations from the normal being no greater than in any series of patients in their age-groups. The findings, on fractional gastric analysis, were also not suggestive, only 11 per cent of patients showing an anacidity after intramuscular injection of histamine. It is well to realize that migraine may, and very frequently does, occur in an otherwise perfectly normal individual, and on the other hand may occur as an entirely independent condition in a person suffering from any kind of disease.

DIAGNOSIS

The diagnosis of allergic migraine must be based upon several findings, as follows:

1. A family history of migraine, or of other allergic manifestations such as asthma, hay fever, urticaria, eczema, epilepsy or periodic attacks of abdominal pains, diarrheas or polyuria.

2. The history of the typical symptoms described above, occurring in attacks lasting from a few hours to several days, often ceasing abruptly and recurring after intervals varying from a day to many months.

3. A history of other allergic manifestations in the past or coincident with migraine. In our series migraine was rarely the only allergic symptom, 89 per cent of the cases showing also other manifestations (Table 7).

TABLE 7. Showing Frequency of Multiple Allergic Manifestations in 150 Migraine Patients.

	Number	*Per Cent*
Migraine as only symptom	16	11
Other allergic manifestations present	97	65
Multiple allergic manifestations present	37	24

4. The exclusion of the possibility that the headache or visual disturbance may be of organic origin, as in the case of eye diseases, dental or sinus infections or cerebrospinal lesions or that the gastrointestinal symptoms may be caused by real pathology in the abdomen or pelvis. This requires not only a thorough general physical examination, but usually careful special examinations of the regions mentioned.

5. The determination of the allergic factor consists in finding a specific food or foods, medication, dust or other inhaled material or gas, bacterial protein, physical agent, or endocrine substance which, when not present in the circulation, will not produce attacks, when again present will produce the typical symptoms, and when then neutralized or eliminated will cause a disappearance of symptoms.

6. The finding of an eosinophilia during the attack is very suggestive. We have found from 3 per cent to 20 per cent or more of eosinophiles in certain patients.

7. The sudden cessation of symptoms in response to a dose of epinephrin given intramuscularly or sublinqually is considered, in other conditions, to suggest an allergic etiology, and in migraine it frequently produces quite a dramatic relief of symptoms, with their recurrence as its effect wears off.

The discovery of the allergic factor is the most important point in the diagnosis, and often proves quite difficult. Some patients have found out for themselves quite definitely that the ingestion of certain foods will always produce an attack of migraine, and many others, when the probability is suggested to them, will say that they have always suspected this to be so, and will be able rapidly to confirm their suspicions. The actual trial of foods by means of test-diets is always the most reliable method of determining the food or foods to which a patient is sensitive, and for this purpose a fixed routine like Rowe's "elimination diets" can be followed, or, starting with a single food or a few foods to which the patient is known not to be sensitive, additional foods can be added until reactions are produced. The reactions may occur soon after the food is ingested or may be delayed for as long as 24 hours. Cutaneous sensitization tests can be performed, but are not uniformly reliable. In the end the determination as to whether certain foods are the allergic factors

consists in the proof that symptoms will never occur except when one or more of these foods are ingested.

Menstrual migraine, occurring at a time when not yet completely understood chemical processes are taking place in the pelvic organs and in the endocrine system as a whole, may easily be due to an allergic reaction resulting from sensitization to one of the products elaborated at that time, such as ovarian hormone or prolan. In some cases a careful history will show that migraine attacks have occurred only at a time of disturbance in a focus of infection, as, for instance, after a treatment for a sinus infection, the scaling of pyorrheic teeth or the occurrence of an acute upper respiratory infection. In such cases the migraine may be due to sensitization to the bacteria themselves or to one or more of the products produced by their action on the tissues.

Migraine occurring after direct exposure to sunlight, to cold or to other physical agents, may occur not only as a reaction to these physical agents themselves, but may be due to sensitization to substances produced by chemical reactions in the skin or other tissues as a result of the action of these agents upon them.

TREATMENT

The treatment of migraine must take into consideration the treatment of the actual attack and the prevention of more attacks. Prophylaxis certainly is the more important part of the treatment.

The treatment of the migraine attack should, of course, consist in the elimination or neutralization of the causative factor as rapidly as possible. Realizing that, in the case of a food-allergy, the offending food has probably progressed a considerable distance down the gastrointestinal tract, lavage of the stomach, either with the tube or by the administration of large doses of warm salt water to induce vomiting, while probably of no direct value in eliminating the offending factor, will often relieve the vomiting which is so frequently a very distressing symptom. Catharsis, by means of castor oil, not only gets rid of the food if it is still present in the intestine, but the ricinoleic acid acts as a detoxifying agent as well, so that it is helpful even though a spontaneous diarrhea already has occurred as a part of nature's reaction to the food poisoning. Early feeding of fairly large quantities of bland food will frequently relieve the persistent vomiting and rapidly will reestablish normal gastrointestinal function, which is often disturbed after an attack of migraine because of combined starvation, vomiting and diarrhea.

The intramuscular or sublingual administration of epinephrin in doses of 0.6 to 1 c.c. of the 1 to 1000 solution will often give prompt relief of symptoms, with later recurrence as its effect is dissipated. A continuous effect may be obtained by giving ephedrine orally with or after the dose of epinephrin, or substituting it for the latter, producing a slower but more prolonged effect. Where these drugs produce too much thyroid stimulation, causing at times quite alarming hyperthyroid symptoms and necessitating large doses of sedatives to counteract this effect, it is better not to use them. In many cases, pituitary extract will give equally brilliant results, without the attendant thyroid stimulation. Rest, and the application of cold or heat, to the head will afford considerable relief, coal tar or other sedatives may have to be resorted to, although their use should be discouraged. As the attack is always self-limiting, it is unwise to risk inducing a habit for the sake of a few hours' less of suffering from the headache.

Prophylactic treatment should consist first, perhaps, in the avoidance of intermarriage between families known to show allergic manifestations, thus avoiding, as far as possible, the occurrence of these so often distressing and disabling conditions. In the individual with migraine attacks caused by food allergy, avoidance of the offending foods will prevent the attacks. As migraine attacks usually occur at fairly long intervals, indicating that the foods causing it are not very often taken by the patient, it is as a rule not necessary to consider specific or non-specific desensitization. Where the food is a common one and desensitization by gradually increasing doses of the food or by the use of the specific peptone of the food *(propeptan)* one-half hour before feedings, is accomplished, it must be borne in mind that in order to maintain tolerance to the food it must thereafter be taken almost daily to prevent recurrence of sensitization. This means practically that it is worth while to desensitize patients only to milk, wheat, egg or potato. In menstrual migraine, gradual desensitization can be produced by continuous and intermenstrual stimulation of the ovaries by means of endocrine therapy. All removable focal infections should be thoroughly eradicated, but where there is a bacterial or tissue sensitivity to irremovable foci, as in the case of infections in the nasal accessory sinuses, desensitization by means of vaccines, filtrates, foreign protein or peptone injections may be attempted. In the prevention of allergic reactions in general, our results from the prolonged use of extracts of the endocrine glands has not been uniformly of value, although at times, parathyroid extract, especially when combined with calcium and with adrenal or pituitary extract, has seemed worth continuing. Where coincident gastrointestinal lesions are discovered, these should, of course, be cared for in the usual way.

The prognosis of migraine should be considered very good so far as the prevention of future attacks is concerned, if the patient is coöperative and will permit the carrying out of the line of treatment suggested. It must be remembered, however, that attacks will always recur whenever the offending factor is again ingested or is allowed again to become active.

SUMMARY

1. The term "migraine" should not be used to designate a group of symptoms definitely referable to an organic cause.

2. Migraine, an allergic phenomenon, is probably caused by a transient edema of the cerebral meninges.

3. The diagnosis of migraine depends essentially upon a history of typical attacks in a patient with an allergic family and personal history and upon the finding of a definite allergic factor.

4. The treatment of the migraine attack consists in rest, sedation, rapid elimination or neutralization of the offending factor and the use of adrenal or pituitary extract.

5. Prophylaxis consists in avoiding offending foods, desensitization where removal of an offending factor is impossible, the removal of focal infections and the restoration of a normal endocrine balance.

DIAGNOSIS AND MANAGEMENT OF GALL TRACT, PARTICULARLY GALL-BLADDER, DISEASE

A PROPOSAL FOR BETTER STANDARDIZATION OF METHODS*

By

B. B. VINCENT LYON, A.B., M.D., SC.D.

PHILADELPHIA, PA.

FORTY years ago, even twenty years ago, there was no plan approaching standardization for the management of gall bladder disease. There had been no serious attempt at prevention of late gall tract disease; that is, the prevention of gall stones and the thick walled gall bladder of chronic infection and inflammation. The prevention of a disease that spreads to the outer coats and produces the adhesively bound-down gall bladder with destroyed function, and leaves a prison which houses the homicidally inclined gall stone, fraught with risks to other associated systems, crippling their efforts to maintain normal secretory and motor function.

That period from 1885 to 1915 marked the general arrival of the abdominal surgical era, which has steadily gone forward, tempered by the law of "trial and error".

Fitz's immortal paper on appendicitis was not published until 1886. Within that same thirty year period, appeared Sippy's most widely exploited method of medically treating peptic ulcer, still too widely in use, a method that has influenced the objective of most surgical procedures for the correction of ulcer, a method based on abolishing free hydrochloric acid in the stomach. Likewise, the greatest book of that period dealing with the gall bladder was published in 1899 by Kehr of Germany and dealt exclusively with gall stone disease and its surgical management. Indeed, at that time, there was no medical management of gall bladder disease worthy of the name.

No wonder that aphorismic slogans were coined, and were taught to and memorized by every young doctor—such slogans as "purgation spells perforation", "no acid, no ulcer", "fair, fat and forty, mother of children, suffering upper abdominal pain and belching gas, means gall stones". At least, the last one of these slogans, interpreted today, should be relabeled to read "late diagnosis".

Much good, however, has derived from them. We have been taught how best to prevent perforative appendicitis and to recognize and remove, or have removed, this useless and dangerous organ before the explosive stage is reached.

Although certain advances have been made in a better understanding of peptic ulcer, the chronic ulcer problem today is still as unsolved as it was thirty years ago. Certainly so, if we view it from the medical standpoint that we must still adhere to the unphysiologic principle of abolishing the gastric juice even if that were medically possible. Or if we view it from the surgical standpoint that we must remove two-thirds of the stomach, followed, at times, by vagectomy, to accomplish that same unphysiological principle, or if we go even a step further and do, as Crile now suggests, remove one adrenal gland and all or part of the thyroid to heal an ulcer no bigger than your thumbnail in an accessible portion of gastro-intestinal canal. That is a long way 'round the mulberry bush, and leaves us a dangerously rickety platform to stand on and say that the "ulcer problem has been solved". How silly it is to affirm it when in the short space of three years there have appeared three newly exploited methods of cure: mucin, citrosalven and metaphen. If it were already solved, why the new methods? We do not mean to suggest that this problem will not be solved eventually, but to express the view that this happy ending has not been yet achieved.

But what about the gall bladder and liver problem which it is our province to discuss? And how might it be presented in simple outline from the standpoint of the general practitioner, the surgeon and the specialist?

For a brief time let us still stick to generalities before developing the topic. First in the way of prevention: if we were to coin some modern slogans, we would say:

1. Avoid typhoid and the enteric group of fevers.
2. Avoid infection in tonsils, teeth, sinuses and respiratory tract.
3. Avoid the incautious use of drugs of the quinoline series.
4. If a woman, avoid having a large family.
5. Eat three meals a day but avoid getting fat.
6. Don't be a "meal skipper" but don't be a glutton.
7. Don't be a Jack Spratt and eat no fat or the surgeon will get your gall bladder before you "know where you're at".

These are some of the simple truths we should teach our patients if we desire them to avoid gall stones and late gall tract disease. It may be "poor business" but it's good doctoring just the same.

Etiology: For a moment let us consider the etiology of gall bladder and liver disease. Boiled down to four points, they are cellular damage, catarrh, stasis of bile and infection. We cannot discuss them fully, but contributing to produce them are dietetic or alcoholic over-indulgence; faulty dieting or meal skipping which "splints" the gall bladder; sedentary living, obesity or marked subnutrition; and the abdominal tumor of the pregnant woman with her increased blood cholesterol. All of these favor, in one way or another, the production of cellular dysfunction, mucosal catarrh and bile stasis. They accelerate the likelihood of infection, and infection, in turn, hastens the onset of chronic disease.

To the gall bladder itself, there are five routes for infection: portal blood, systemic blood, lymphatic circulation between liver and gall bladder, ascending infection from the duodenum, and direct peritoneal contact through adhesions from inflamed neighborhood viscera. We believe that the mucosal portal of entry to infection is far more common than is the serosal (lymphatic circulation) because otherwise pericholecystitis should be seen as an early rather than late stage of the disease. Others disagree with our view, but our's has been steadily reinforced by the evidence to be found in a study of the bile itself in both early and late gall bladder disease.

Have we now a standardized plan for the management of gall bladder disease? Not yet one in which we are all in agreement, but a far better one than we had twenty years ago. And what series of events and what men have we to thank for it? The surgeon, the pathologist, the physiologist, the experimental-animal laboratory worker, the roentgenologist, the clinician, the informed family physician, and the gastro-enterologist, all aided by the march of time.

Just think back. Although Petit, the great French surgeon, in 1794 conceived the idea of surgically removing gall stones, the first authentically-known operation in America upon the gall bladder itself was done in 1867—only sixty-six years ago, one year after the Civil War—and done by an obstetrician named Bobbs of Indianapolis, and because of a mistaken diagnosis. He thought he was

*Presented before the Philadelphia County Medical Society's Postgraduate Seminar.

opening the abdomen for an ovarian cyst and wound up by doing the first cholecystotomy—without the preliminary preparation as advised by Petit—on a huge hydrops of the gall bladder.

This started the surgical ball rolling. But nearly twenty-five years were to elapse before any surgeon dared to remove the gall bladder, and even after forty years had passed, we find that no less an authority than the late John B. Deaver warned against it and in 1908 wrote in his vigorous fashion "This question of cholecystectomy appeals to me strongly, as I fear, from what I read and hear, the practice is all too common and the influence of this teaching upon those who have not themselves had sufficiently large experience to decide for or against removal, will be bad indeed. My experience is that the more surgery I do the less inclined I am to remove the gall bladder." How well the author remembers it for he was a cub assistant of that distinguished surgeon at that very time!

But time marched on. Deaver and others became converted to cholecystectomy, and in the period between 1916 and 1920 he performed it 611 times out of 800 patients operated for gall tract disease. So, with increasing experience the surgeon, aided and stimulated by the pathologist, the physiologist, the roentgenologist, and the oft-maligned vivisectionist—and may he long be spared—taught us much. Their views were tempered by that lustily growing infant, the gastro-enterologist, who, even twenty years ago, rapidly had become bed-broken and had discarded his diapers.

Between them all, they taught us that gall bladder disease, even gall stone disease, is common in young adults, is by no means rare in children and occurs even in infants. So the "fair, fat and forty" aphorism meant *late diagnosis* and became outmoded because it was only true of the more characteristic clinical explosions of late gall tract pathology. The breeding or quiescent period for such disease may have begun ten to thirty years before. It is now up to us to recognize this early stage, to correct it and thus prevent late pathology. This is the medical stage which will yield to modern medical methods if properly applied.

Gall stones, the chronic thick walled functionless gall bladder, with the adhesions of pericholecystitis, the rare instances of cancer or other neoplasm of the gall bladder are surgical and only surgical.

Between the two extremes fall many gall bladder patients who are borderline and selection of the plan of management for each requires good judgment. Many may be kept well throughout their lives by proper medical tactics —perhaps equally as many will require surgery sooner or later, and in this group the sooner the better. But all patients after operation should be placed on a standardized medical regime to see that they stay well.

Although "fair, fat and forty" is out of date in more ways than one, it is still true that women are more subject to disturbances of the gall bladder than are men, because the pregnant women usually doubles her blood cholesterol and thus increases her risk of forming cholesterin gall stones, due to this disturbance in metabolism and not because of infection. Hence, there is a danger in multiple pregnancies, although the religionist may object to the idea. Thus, gall bladder disease in women, and often young women, reverses the duodenal ulcer ratio in which men are four to five times more frequently afflicted. Unhappily cholecystitis and peptic ulcer occur very frequently in the same patient and this sometimes complicates the choice of management.

Owing to the enormous amount of research upon this subject that has occurred during the last twenty-five years, it is now more generally accepted that disease of the gall bladder or of some part of the biliary system is more responsible for the occurrence of various symptoms of indigestion than is any other intra-abdominal organ or disease picture, not excluding appendicitis, gastric or duodenal ulcer, colitis or intra-abdominal cancer. At times, it can symptomatically mimic them all. Moreover, it can also mimic cardiac disease or coronary artery disease and when both are present, it is often difficult to decide which is more responsible for the abdominal, chest and back pains. Therefore, the gall bladder should be studied in all cases of dyspepsia.

During this twenty-five year period, the four outstanding advances in diagnosis have been the introduction of the modern duodenal tube in 1909; of biliary drainage by the duodenal tube in 1919; of cholecystography in 1924 and of a group of liver function and other laboratory tests. Each of these last three maneuvers supplement one another and yield certain diagnostic evidence not furnished by the others, and when added to a well-taken history and a well-done physical examination—the foundation stone of all diagnosis—will enable us to recognize and to classify gall bladder disease as medical, surgical or borderline. Biliary drainage by duodenal tube has great therapeutic merit in the management of both gall bladder and liver disease and this value we shall indicate.

Here we might mention one important point of difference in the management of appendiceal disease and gall bladder disease. So far as we now know, the appendix has no function and, because this is so, it frequently and seriously jeopardizes health and life. It is "in season" the year round to the surgeon and rightfully so, just as are predatory animals and birds to the hunter. But the gall bladder has a function, in fact several functions, in the storage, concentration, and delivery of bile, as well as in the absorption of certain chemical constituents of the bile, although the ultimate fate of all of these constituents is not yet known. Since the gall bladder has a definite function it should, if possible, be preserved to the body as a whole. If its function is diminished but not destroyed, attempts should be made by medical tactics to improve or restore it. If its function is entirely destroyed, if it can no longer store, concentrate, absorb, and empty the bile, because of chronic inflammatory disease or infection, because of advanced gall stone disease, or adhesions, or because of cancer or other neoplastic new growth, it should be speedily removed by the surgeon in the interest of the body as a whole. And this is especially important in protecting the health of the liver, the heart and, to a less extent, the kidneys. We have the surgeons particularly to thank for spreading this truth, even though in certain sections, they have overdone it a bit, but only because of their earnest enthusiasm to have it "register".

What are the diseases of the gall bladder itself or those associated with other components of the biliary system? There are two disorders or dysfunctions and twelve gradations of organic diseases of the gall bladder that we shall briefly review. Each might quite legitimately furnish material for an hour's discussion. Our main object is to attempt to influence you to adopt a more standardized plan of recognition and particularly of treatment.

The two gall bladder and duct dysfunctions are:

1. Spastic dysfunction or distension.
2. Atonic dysfunction or distension.

The twelve diseases of the gall bladder and biliary system are:

1. Early cholecystitis with unobstructed cystic duct. Simple catarrhal cholecystitis.
2. Early cholecystitis with obstructed cystic duct due to catarrh.
3. Cholecystitis, with cystic duct obstructed from stone, adhesions, stricture, tumor.
4. Cholesterosis of the gall bladder: "Strawberry cholecystitis".
5. Hydrops of the gall bladder: "Mucocele".
6. Acute infective cholecystitis, with and without obstructed cystic duct.
7. Acute suppurative cholecystitis and chronic empyema.
8. Neoplastic disease of the gall bladder, malignant or non-malignant.
9. Constitutional disease affecting the gall bladder: Tuberculosis and syphilis.

10. Parasitic infestation of the gall bladder.
11. Chronic non-calculous cholecystitis, with and without complications.
12. Gall stone disease, with and without complications.

Dysfunctions of the gall bladder and extra hepatic ducts. The possibility that disorders of motility of the extra hepatic biliary system actually exist has been suspected for many years and some clinicians have noted the occurrence of liver and gall bladder pain with absence of structural disease. Newman in the 1933 Goulstonian Lectures is the last to direct attention to this neglected topic.*

It is almost axiomatic that functional derangement usually antedates, and certainly predisposes to, organic structural change of the gastro-intestinal tract and its appendages. Their common innervation, derived from the vagus nerve and the sympathetic system, suggest the possibility of a unity of functional disorders occurring with biological alterations of *habitus*. Much study has been given functional disease of the stomach, intestines and colon but scant attention has thus far been given to its probable existence in the gall bladder and extra hepatic ducts. Therefore, Newman's review of this probability, coupled with a careful reëxamination of the known facts concerned with the physiology of the biliary system, has led him to describe a condition which he calls "biliary dyskinesia".

Some years ago we alluded to atonic dysfunction of the gall bladder and to spastic painful phenomena and in the author's book he described some case histories which seemed to support the theory. Smithies, Karshner and Oleson also suspected disturbances of function due to a blocking off of nerve stimuli to gall bladder, ducts or sphincter. They selected the term "physiologic block" to describe a failure of the normal neuromuscular reflex concerned in bile excretion properly to function. Newman describes functional disturbances anew under titles of "spastic distension" which is quite common, and "atonic distension" which, in his experience, is quite rare. Up to the moment, we believe we have seen more instances of the atonic than of the spastic variety.

Newman feels that there are biological differences in the subjects which tend to predispose them to one or another of the two principal types of dysfunction. It would require a separate paper adequately to describe them. Suffice it to say first, that much greater attention should be devoted to their recognition, and second, to indicate that, after recognition, their treatment should follow medical rather than surgical tactics.

Meltzer's hypothesis as to the reciprocal innervation of the gall bladder and of Oddi's sphincter and the ampulla of Vater was questioned for many years because of discrepancies in experiments by physiologists. Apparently this was because of the strength of, not the character of, the stimulus used. Westphal seems to have cleared up this difficulty by showing that *light* stimulation of the vagus (chiefly the left), whether by electricity or by drugs, contracts the gall bladder, relaxes the sphincter of Oddi, and causes peristalsis of the ampulla of Vater and a flow of bile. Whereas, and secondly, *strong* stimulation causes spasm in both gall bladder and ampulla and cessation of flow. On the other hand and thirdly, stimulation of the splanchnic sympathetic nerve causes relaxation of both gall bladder and ampulla and contraction of Oddi's sphincter.

The second factor may be operative, and may explain the causation of pain, in spastic dysfunction or distension of the gall bladder. It may be severe enough to mimic gall stone colic, although the pain is as a rule not so severe. In the author's book*, ten years ago, he suggested that the cause of pain might be due to simultaneous contraction of the gall bladder acting against a spasm of the ampulla with a consequent rise of intraduct tension. If the mucous membrane of gall bladder or ducts is already inflamed the pain is just that much greater.

The third factor may explain the dull pressure-ache or sense of fullness in an over-distended gall bladder that cannot empty against a closed or contracted sphincter of Oddi and thus becomes muscularly more and more atonic†.

Theoretically the *spastic group* calls for sedation and temporarily lessened emptying effort until relaxation of the ampulla is controlled by vagal inhibition; the *atonic group* calls for exercise of gall bladder emptying, plus vagal stimulation and sympathetic sedation. Practically speaking, we treat both groups the same since we have no drugs that ideally produce vagal stimulation and sympathetic depression at one and the same time. But, as in spasm of other parts of the gastro-intestinal tract, we use tincture of belladonna to full physiological effect in cases we suspect spastic dysfunction of the gall bladder and duct system, but omit it in the atonic variety.

Treatment of Spastic Dysfunction. Newman finds satisfactory results follow diet and medicine. He advises *diet* consisting of small, equal and regular meals, four times a day, but avoiding mixtures of starches and fats, and a generally smooth and non-irritating diet. *Medicinally*, he recommends tincture of belladonna in ascending dosage sufficient to physiologically produce vagal inhibition. This varies with the individual. To this is added fifteen grains of sodium bicarbonate, with infusion of rhubarb as the vehicle. In this group we also make use of therapeutic duodenal tube drainages.

Treatment of Atonic Dysfunction. Contrary to Newman's dissatisfaction with the treatment of this condition, our own results have been as satisfactory as in the spastic group. The method we use is as outlined in the three item plan to be later described as the medical tactics for catarrhal cholecystitis with unobstructed cystic duct, and with cystic duct obstructed by catarrh. When Ivy's gall bladder-emptying hormone—cholecystokinin—is purified sufficiently for human administration intravenously, this should certainly be a most useful adjunct to medical management.

This subject of functional disorder is too important to dismiss with such brevity but space does not allow further development.

1. *Early cholecystitis with unobstructed cystic duct. "Simple catarrhal cholecystitis."* This is the stage of catarrhal and low grade inflammatory reaction, with low grade or no infection, and this is the breeding period for late gall tract disease. This stage is purely medical. If untreated or improperly or inadequately treated, it may become chronic, punctuated by frequently recurring mild or subacute exacerbations.

During this quiescent period there may be no symptoms referable to the gall bladder itself except an occasional pin-like darting pain, a momentary soreness or aching or a sensation of fullness in the region of the gall bladder. More often, there is simple "indigestion", with reflex symptoms referred to the stomach, such as belching, epigastric distension, pyrosis, mild nausea. These are frequently due to disturbance in gastro-duodenal secretion and motility. Bile regurgitated into the stomach may be the actual cause of the nausea. The regurgitation may be due to an associated low grade gastro-duodenitis, with an irritable duodenum reversing the peristaltic wave.

Physical signs are absent or negligible except for general epigastric region soreness. The gall bladder is never palpable and the region may not be tender. The cholecystographic response is normal. Laboratory examinations of blood, urine and stool are normal.

The only definite evidence is afforded by a gross and microscopic study of the bile sequence obtained by duodenal tube study, by culture study and by chemical study of the bile, the latter too incomplete as yet to discuss here.

*Newman, Chas.: Goulstonian Lectures, Lancet, April 15, 22 and 29, 1933.
*Non-Surgical Drainage of the Gall Tract; Lea and Febriger. See pp. 572 to 578.
†Ibid. See pp. 517-522; 539-542; 545-547.

At this stage, there may only be alterations in the composition of the gall bladder bile which becomes thicker, more viscid and contains increased flocculi microscopically showing the products of catarrh and inflammation, mucus, pus cells, desquamated epithelium, perhaps an occasional bacterial colony, and rarely a slightly increased crystalline deposit. By analogy, examination of the bile itself at this stage stands in the same relation to late gall tract disease as the finding of a trace of albumin, a change in specific gravity, a few casts in the urine does to kidney disease. Why wait for Bright's classical description of anemia, edema, a failing heart and anasarca in order to complete the terminal picture? Educate the patient how to live and treat it early and Bright's disease, gall stones, chronic adhesive cholecystitis and the terminal picture of hepatic cirrhosis may become as infrequent as typhoid fever.

We rarely ever get an opportunity to study the histopathology of this earliest stage of cholecystitis because few die or come to autopsy. Probably the only alteration in the gall bladder would be mild edema and catarrhal inflammation of the mucous membrane. This stage, as we have stated, is purely medical. Not only will recovery take place, but prevention of more serious pathology will be achieved by the following three-item plan of treatment.

The essential factor is seeing to it that the gall bladder empties itself normally three or four times a day. Thus bile stasis, cellular dysfunction, mucosal catarrh and the likelihood of localized infection are reduced to a minimum.

A. Dietetically:

Since the gall bladder physiologically empties itself as a result of food stimulus and since we now know that the foods which accomplish this are the fats (and to a less extent proteins, if there is normal gastric acidity) a fat-full diet should be issued. Protein, starch, carbohydrates and vitamine values can be kept at the average unless there are some special indications for increasing or lowering them. The best fats are the simple ones—butter and olive oil of good quality, cream, bacon, occasionally ice-cream, and yolk of soft-cooked eggs. Fried greasy foods are harmful. There should be no meal skipping—three or four meals a day, regularly spaced, and containing some fat are the main need. Two teaspoonsful of olive oil with two or three buttered crackers at bed time may substitute as the fourth meal.

B. Medicinally:

3 to 5 minims of oleic acid in gelatin capsules, one hour before meals or three hours after meals, has been proved by cholecystography to assist in emptying the gall bladder. Or 1 to 3 grains each of sodium oleate, sodium glycocholate and sodium salicylate, to which is added 1 minim of peppermint oil, in a soft mass pill, is a good combination taken after meals. If a laxative is required one-third grain phenolphthalein may be added. If there is pylorospasm, a capsule containing one-five-hundredth grain atropine sulphate or preferably one-sixty-fourth grain atropine valerianate (Clin), one-eighth grain luminal or one-fourth grain barbital, and 3 to 5 grains sodium bicarbonate taken thrice daily before meals is an excellent combination.

C. Technically:

Biliary drainage treatment by duodenal tube according to the author's standard technique, once or twice a week in courses of four to six, and repeated, if necessary, two or three times a year, will keep the cystic duct patent and the gall bladder bile from stasis, as well as having a desirable stimulating effect on the liver cells and on the gastro-duodenal mucosa.

2. *Early cholecystitis with obstructed cystic duct due to catarrh.* As we pointed out in a paper published with Dr. W. A. Swalm in 1927, catarrhal obstruction of the cystic duct is of common occurrence, but without duodenal tube examination it escapes recognition. It may be partial or complete. If not recognized at an early stage and adequately treated, it leads to more advanced grades of cholecystitis and we believe may have something to do in accelerating a cholesterosis of the gall bladder. When associated with early cholecystitis only, it does not give a characteristic symptomatology although the sensation of fullness, aching, or momentary pin-prick pain in the region of the gall bladder may be more pronounced because the cystic duct is obstructed. This form of cystic duct obstruction can be differentially diagnosed from other forms only by biliary drainage study, controlled by cholecystography and by the course of events after the patient has been followed up for a time.

Its presence is indicated by a characteristic macro- and microscopic alteration of biliary drainage aspirates. Either no gall bladder bile is recovered or only in small amounts, and accompanied or preceded by the discharge of flocculi of yellow to greenish mucus in shaggy, slimy masses. This mucus is unusually dense, microscopically is frequently seen to be twisted or spiraled and encrusted with what appear to be bile salts. And most important, there melts out from this mucus an oleaginous material in droplets, pools and lakes ranging in color from pale greyish yellow to a brilliant golden yellow. This lipoid, to chemical tests, seems to be a fatty ester of cholesterol.

Because the cystic duct is obstructed, the dye used in cholecystography fails to reach the gall bladder, therefore, no shadow or merely a faint shadow of the gall bladder is visualized and this comparatively simple condition is quite frequently misdiagnosed as a surgical degree cholecystitis and the patient may be needlessly explored or even cholecystectomized. This accounts for many of the cases in which operation was performed on the basis of a "positive" cholecystogram but in which the surgeon was unable to demonstrate disease of the gall bladder. This error is avoidable.

Patients wth cystic duct catarrhal obstruction, if *unassociated* with other pathologic change, do not require surgery but will regain normal gall bladder function by means of biliary drainage treatment, as proved by control cholecystography. Usually six to twelve treatments will suffice. When the obstruction has been overcome, the patient may return to the fat-full diet to which he had previously been intolerant. An occasional gastric lavage of the stomach, particularly if bile is regurgitated, is most helpful in correcting the gastro-duodenitis and the patient's most disturbing symptom—nausea. The medicinal treatment is the same as in early cholecystitis with patent cystic duct.

But if there is associated pathology approaching Grade III cholecystitis or a cholesterosis, or if the obstruction has been of long enough duration to produce hydrops, surgical correction—a cholecystectomy—should be carried out. All other forms of cystic duct obstruction are likewise primarily surgical.

3. *Cholesterosis of the gall bladder.* This is a mild but common form of cholecystitis and in about four per cent of cases the mucous membrane may contain papillomas or adenomas. The mucous membrane is congested, reddened and studded with innumerable yellow specks or streaks where the lipoid cholesterol has been deposited within and beneath the villi. This contrast of the red mucous membrane with its yellow dots makes this condition popularly called "strawberry cholecystitis". Gall stones may or may not be present but when present are generally of the "pure" cholesterin variety. The cystic duct at first remains patent; later on, it may be obstructed by the oleaginous material above described. The external gross appearance of the gall bladder may be normal, although if the wall is very thin the yellow spots may be faintly visible. The gland near the cystic duct is frequently found enlarged.

There are no diagnostic symptoms which are characteristic of cholesterosis itself. There may be none; they may be those of mild cholecystitis. But if acute or chronic cholecystitis occurs concurrently, or, if there are stones present, there may be more severe upper right quadrant pain, referred to shoulder blade or back, or typical biliary colic, mild jaundice and mild fever. If the cystic duct is occluded even without stone impaction, there may in some cases be as severe colic as in calculous cholecystitis.

In uncomplicated "strawberry gall bladder" the cholecystogram will show no deviations from normal concen-

trating function and emptying capacity because neither is altered. When chronic cholecystitis has occurred the cholecystogram will suggest it. An increased blood cholesterol has been thought to be more constantly high in cholesterosis, and therefore of diagnostic value, but in Illingworth's fine study of a number of cases on Professor Wilkie's service in Edinburgh, an increased blood cholesterol was as frequently found in the control cases as in those with cholesterosis.

The main point to remember is that when cholesterosis is discovered, the treatment is surgical, since the chief importance of this form of gall bladder disease is that it favors the development of gall stones, and the development of chronic cholecystitis. Since the disease is within the submucous layers of the gall bladder, neither surgical nor medical bile drainage can accomplish as much as will cholecystectomy. After operation, however, as in the other surgical groups, the patient should be placed on the standard follow-up treatment.

4. *Hydrops or mucocele of the gall bladder.* When the cystic duct has been completely obstructed for a sufficient length of time, whether by stone impaction, catarrh, stricture, by malignant disease or by pressure from without, no bile flows in or out of the gall bladder and the latter becomes distended with mucus, at first mixed with bile, but later pigments and bile salts are absorbed or disappear, leaving so-called "white bile". If chronic cholecystitis has not thickened the wall, it may distend to paper thinness and the hydropsical tumor may grow to large size, contain a quart or more of fluid and may be mistaken for ascites or ovarian cyst as in Bobb's historic case.

In the earlier stages, there may be attacks of painful spasm in the region of the gall bladder sometimes severe enough to resemble biliary colic; indeed, if due to cystic duct stone impaction, an actual biliary colic. Nausea and persistent vomiting are frequent but jaundice is uncommon. Later on, when the gall bladder can no longer contract, the condition may be comparatively painless and be recognized only by abdominal examination.

The most important diagnostic point is the palpably enlarged gall bladder which moves down with respiration and can be displaced laterally but not downward, and thus can be differentiated from a movable right kidney or a hydronephrosis, the more readily so because the tumor is immediately beneath the abdominal wall and not deep-seated. It may not be tender if the inflammation has subsided. It may be resonant to percussion. The treatment is surgical and requires cholecystectomy.

5. *Acute infection cholecystitis.* The milder cases may follow a descending acute hepato-cholangitis or ascend by extension of a simple catarrhal cholangitis, so-called catarrhal jaundice. They frequently accompany infectious fevers like typhoid, pneumonia or influenza as we have observed on studying the bile during epidemics. In such cases the icterus index and van den Bergh tests are often positive, with increased bilirubin in the blood serum. The presence of cholecystitis may be suspected by finding tenderness over a gall bladder that may sometimes be palpably enlarged. Cholecystography too frequently yields a normal response and is of less value than in chronic cholecystitis. Duodenal drainage evidence is more helpful because in acute cholecystitis the mucous membrane is chiefly affected and becomes inflamed, spongy, edematous and desquamates its lining epithelium. Thus, at microscopy, we find increased bile stained pus cells and masses of exfoliated cells, characteristic of gall bladder derivation, in the overabundant flocculi. Bile stained bacterial colonies will usually be found and cultures made from the bile will often identify the nature of the infection.

The patient loses appetite, has nausea, pain and mild fever. Vomiting may occur. The upper right rectus muscle may be spastic and irritable and the gall bladder tender. As the attack subsides, soreness replaces pain and tenderness.

A high appendix "pointing north" may confuse the diagnosis. Indeed, both may be present. The leucocyte counts are higher as a rule in appendicitis. If the latter is present, surgery is required. Herpes zoster may sometimes mimic the picture and here surgery is to be deplored.

The *general treatment* of acute infected cholecystitis is expectant: bed rest, ice bag, liquid diet, supportive measures, care of the bowels, occasionally morphine.

The *special treatment* is designed to secure adequate drainage and disinfection of the inflamed organ. At this stage surgery is usually not indicated since most cases subside after a week to ten days, with duodenal tube drainages given daily or every second day, and with the administration of large doses of sodium salicylate and hexamethylenamine (urotropine or uritone). The latter liberates formaldehyde which passes out through both liver and kidneys. It may be detected in the bile recovered by drainage. Hurst of Guy's Hospital, London, advocates large doses, 50 to 100 grains, of hexamethylenamine three times a day, protecting the kidneys by giving at the same time 60 to 100 grains each of sodium bicarbonate and sodium citrate to keep the urine constantly alkaline. Some believe, however, that formaldehyde is not liberated with an alkaline urine.

After the acute phase has subsided, the patient is temporarily given a cholesterol-low diet but otherwise the same follow-up management as in simple catarrhal cholecystitis. It should be more prolonged, however, since one attack of acute cholecystitis untreated is followed by others and *favors gall stone formation and chronic cholecystitis.* Vaccine therapy may help, and in many cases with pyogenic bacteria, does help to control the possibility of reinfection.

6. *Acute suppurative cholecystitis and chronic empyema.* If the acute attack is the result of a virulent infection, the mucous membrane becomes greatly inflamed, minute ulcers may form, and, if the condition gets out of hand, may pass rapidly into a gangrenous suppuration. The cellular products of inflammation predominate in the drainage microscopy and the catarrhal becomes a purulent exudate leading to chronic empyema of the gall bladder if the attack subsides.

There is increased severity of the constitutional symptoms with higher temperature and pulse rate; higher leucocytosis, fever, sweats and prostration, greater localized abdominal rigidity and increased danger of perforation with resultant local or general peritonitis, exactly as in suppurative or gangrenous appendicitis. If gall stones have formed as a result of previous attacks, the perforative threat is greater.

After the diagnosis is made, or even if such a situation is suspected, the patient should be immediately hospitalized and the selection of the day or hour for surgery given careful consideration. If the attack shows evidence of subsiding, it is better to wait, but the surgeon's hand may be forced to quick intervention. Duodenal tube treatment should *not* be considered if the signs point to gangrenous suppuration. If, however, the process subsides to a chronic empyema and the cystic duct is patent, we have successfully drained an ounce or more of pus from the gall bladder by duodenal tube. In selected cases, with bad hearts or kidneys, this is good judgment, for it paves the way to safer surgery, prepares the operative field and allows the surgeon to do a cleaner cholecystectomy and avoids the two-stage procedure of cholecystostomy followed by cholecystectomy.

After operation the patient should be returned to the standard follow-up, and in 6 to 10 weeks, duodenal tube studies should again be made to see that there is no residual infection in ducts or liver, or if found, to treat it in time and thus lessen the likelihood of subsequent surgery be-

coming necessary. An amazing reduction in post-operative morbidity will follow the adoption of these tactics.

7. *Malignant neoplastic disease of the gall bladder.* Although cancer of the gall bladder is a most important disease, in this paper it must be dismissed with great brevity.

It is a rare disease, far more so than we used to think. The larger the series of cases, the lower the incidence of cancer. Among a thousand cases of gall bladder disease in Smithies' series there were only twenty-three cases (2.3 per cent) of primary and eight (0.8 per cent) of secondary malignant disease. In the nearly seventeen thousand gall bladders operated at the Mayo Clinic up to 1929 Judd and Baumgartner report that only 0.5 per cent had cancer.

There has been thought to be a definite etiological relationship between gall stones and cancer of the gall bladder but some additional factor seems necessary. Rolleston finds that stones are present in the great majority of cases, but that cancer occurs in only a small percentage of all gall stones cases. It is more common in women.

The symptoms may be those of a preëxisting cholelithiasis, or those of a local invasion of the gall bladder or those of complications as metastases to other organs take place. Jaundice may be present. Ascites occurs in 25 per cent of cases because of liver involvement. Fistulae may occur.

Diagnosis is very difficult and rarely possible in the early stage unless incidentally detected at laparotomy for gall stones. Rolleston points out that it may be suggested in a woman of middle age with dull upper right quadrant pain, poor appetite and loss of weight, in whom a hard, nodular mass in the region of the gall bladder may be palpated. A distinct shadow to non-dye X-ray is of diagnostic value.

The prognosis is poor. Theoretically treatment is purely surgical and calls for removal, but the expectancy of life thereafter is rarely longer than a year even when matastases have not occurred. Blalock of Johns Hopkins in reporting forty-two cases felt that operation merely served to hasten death, no patient being traceable alive after one year. The high operative mortality of eighteen to twenty per cent in large series is usually due to hemorrhage. The best prognosis occurs in early cases accidentally discovered at gall stone operation. The medical treatment is purely palliative.

8. *Non-malignant neoplasms.* The prognosis for non-malignant neoplasms of the gall bladder is excellent if recognized early and the gall bladder is removed. Such neoplasms are adenomas, papillomas, fibromas, myomas and mixed varieties. They occurred in 8.5 per cent of seventeen thousand gall bladders surgically removed at the Mayo Clinic. They are recognized best during life by the cholecystographic technique proposed by Kirklin. The treatment is wholly surgical.

9. *Constitutional disease of the gall bladder.* Tuberculosis and syphilis of the gall bladder itself is rare indeed—the latter particularly so. There is no method of diagnosis except accidental discovery. Why the gall bladder is immune whereas the liver is frequently invaded, especially by syphilis, should intrigue someone and might repay further research.

10. *Parasitic infestation of the gall bladder.* In Asiatic countries *Distomiasis*, or liver flukes quite frequently invade the bile ducts and occasionally the gall bladder. Elsewhere it is a rarity. More widespread, but not with greater frequency, *ascaris lumbricoides* or round worm may do likewise. *Hydatid cysts* scarcely ever arise in the gall bladder itself, but when they do so are believed to reach the gall bladder in the embryo stage by way of the portal blood stream and the cystic duct. Such conditions therapeutically offer both medical and surgical problems. *Lamblia or Giardia intestinalis*, common enough in the duodenum, may reach the gall bladder by ascent or possibly by way of the blood, and may nest and breed there. Since 1925 a number of cases are on record in which they have been found in the gall bladder. It is a waste of time to medically treat the duodenal infestation if a breeding center is in the gall bladder. *Endamebae histolyticae* have been shown at operation by Smithies* to maintain themselves in the gall bladder and to produce characteristic ulcers. The significance of this is of great importance not only with regards gall bladder damage, but because such "hidden foci" may account for the recurrence of colon lesions or make these patients dangerous "carriers".

Differential diagnosis. At this point and before discussing the large subject of chronic cholecystitis we might emphasize some of the obligatory items in physical examination which should be done in every case of acute gall bladder disease or the acute exacerbation of chronic cholecystitis, if we are to avoid errors in differential diagnosis.

In addition to the usual attention to the upper abdomen and especially to the right upper quadrant, such examination should include equally careful examination of the lower right and left quadrant, the pelvic region, the rectum, vagina and prostate; of the liver, spleen and kidney regions for tenderness or alterations in size or position; and careful examination of the lung bases for pneumonia, pleural fluid or friction rub and free diaphragmatic excursion; and of the costal cage to exclude intercostal neuritis or an early herpes zoster. It should include careful examination of the heart, arteries and blood pressure for evidence of valvular disease, toxic myocarditis, cardio-circulatory asthenia and for possibilities of aneurysm, angina or coronary sclerosis. In addition such examination should include a quick appraisal of the *habitus*, whether visceroptotic or apoplectic; inspection of the sclerae and palate as well as the skin for jaundice; of the lips and mucous membrane for cyanosis or anemia; of the tongue; of the gums for lead line, pyorrhea or aphthae; of the teeth, tonsils and sinuses for focal infection and not forgetting the deep reflexes and Romberg's test.

Even such a skeletonized examination can be routinely done in half an hour and guards us against diagnostic errors. Especially is this true in cases which suggest atypical biliary colic. We can all remember an occasional case of simultaneously active cholelithiasis and visceral crisis of syphilis; or of renal colic, pyonephrosis, Dietl's crisis and Hunner's disease; or associated with pneumonia or acute right-sided diaphragmatic pleurisy; or cases of angina or coronary sclerosis with predominant abdominal symptoms. Unless we are alert we may recognize the one and miss the other.

Also differential diagnosis will be aided, by suitable studies of the urine, stool, blood and stomach and, if need be, the spinal fluid; studies, whose relative values I have no time to discuss.

11. *Chronic cholecystitis, calculous and non-calculous.* In order briefly to cover as much ground as possible in a discussion of the many clinical aspects of chronic cholecystitis and of liver disease, it is best to consider gall stone and non-gall stone disease conjointly instead of separately.

Aside from the acute metabolic gall stone in the young pregnant woman and the acute infection gall stone of some typhoid patients, both represent late gall tract disease that should be preventable if we can learn to recognize the warning signals as merely suggested in the foregoing sections. Once the definitely chronic stage is reached the final therapeutic cure is secured only by surgical procedure aided by adequate medical measures directed toward lowering operative mortality and lessening post-operative morbidity. As a rule cholecystectomy is the preferable operation with exceptions which we shall later mention.

*Smithies, Frank, Annals of Internal Medicine, September, 1930.

Many variant clinical pictures of the disease present themselves depending on whether we are dealing with:

a. Chronic cholecystitis, with infection in the wall, and with patent cystic duct.
b. Chronic cholecystitis, with obstructed cystic duct, usually leading eventually to the small contracted thick walled gall bladder.
c. Calculous or non-calculous cholecystitis with preserved or partialy preserved function or with destroyed function.
d. Calculous cholecystitis with stone or stones in cystic duct or in common duct.
e. Pericholecystitis with adhesions to liver, duodenum, stomach, hepatic flexure of colon, omentum, or elsewhere.
f. Chronic cholecystitis complicated by liver disease; by jaundice; by cardio-vascular-renal disease; or by gastro-intestinal disease.

Even this chronic phase of gall bladder disease is too large fully to discuss. We can merely outline some of the more important points.

Some points in diagnosis: In the upper quiescent stage abdominal gaseous or fermentative dyspepsia, with belching, chiefly after meals, is most frequently complained of. Next in frequency comes epigastric pressure from gastric distension which so encroaches on the cardiac area as to embarrass heart action, often to an extent that when gall bladder pain or soreness are not conspicuous the case may be considered primarily cardiac. Both conditions may coexist. Dull pain or soreness under the right rib margin is next in frequency and, if adhesions are present, referred to shoulder blade, back or mid-abdomen depending on which structures are adherent to the gall bladder. All three of this group of symptoms are intensified when the patient becomes intolerant to fat foods, and particularly so if the cystic duct is obstructed and free drainage of the gall bladder is prevented. Most gall bladder patients themselves first notice fat food intolerance and are apt to volunteer the statement.

If stones are present and attempt to pass through the cystic duct or if an acute exacerbation occurs with obstructed cystic duct or with spasm at Oddi's sphincter as the non-calculous gall bladder attempts to empty itself, the typical pain of biliary colic may occur, and may be so severe that several hypodermics yield little relief of pain, nausea or vomiting. Such colic attacks are more apt to occur three to six hours after the evening or heaviest meal of the day or during the early morning hours, and we are often called out of our bed to the bedside of the patient. This is the usual rule, but we have not infrequently seen an attack start after breakfast. Much depends on whether the food eaten is of a type to call forth a contractile effort of the gall bladder.

The smaller stones are more apt to cause colic since they can enter the cystic or common duct. Frequently after an attack a stone or stones may be found in the sieved stool; this clinches the diagnosis. If the stone is facetted it usually indicates that others are left behind. If much olive oil has been used—as in certain outmoded cures—one must differentiate soap stones from actual gall stones if found in the stool. A large solitary calculus in a small contracted gall bladder cannot pass through the cystic duct but rarely may rupture into the duodenum or colon through an adhesion pathway.

After an acute colic the right upper quadrant is tender, with muscle spasm and rigidity and the entire epigastrium may be sensitive. In the interval between attacks, physical signs may be absent or if the gall bladder region is only slightly sensitive Riesman's ulnar concussion test will best elicit it. If adhesions are present, the tuning fork test we have described will be positive and we believe it as reliable evidence as that afforded by X-ray study.

If a stone impacts in the cystic duct the gall bladder sooner or later becomes palpable. If a stone lodges in the common duct so that it does not completely obstruct, but acts as a ball valve, chills, fever, sweats, attacks of colic and partial or complete jaundice occurs. The intensity and duration of jaundice varies, but usually clears under observation and thus may be differentiated from the constant jaundice accompanying stricture, cancer of the terminal portion of the common bile duct, or cancer of the head of the pancreas. The presence of jaundice, either skin or scleral, and well defined telangiectases above either or both costal margins will always suggest gall tract disease (gall bladder, liver or liver-spleen) and one or another of the many tests for liver dysfunction or liver disease will be positive.

The tests most commonly employed are the following: The *bromsulphalein dye*, the best for testing excretory function. The *icterus index* and *quantitative serum bilirubin* are best for measuring the degree of jaundice and detecting the latent stage. The *van den Bergh* and the *galactose tests* are best for differentiating toxic from infective hepato-cholangitis. The galactose test is of value only when positive and then represents hepato-cellular damage, or parenchymatous disease in the early stage. It may too often be negative if done after the first two weeks of illness when regeneration has begun. The *urobilinogen test* is chiefly useful in differentiating between complete and partial obstruction of bile flow but does not differentiate whether the obstruction is due to extensive cellular liver damage or to mechanical conditions involving the ducts, such as stone or cancer. But when the obstruction is complete no urobilinogen will be found because no bile is entering the intestine to form it. *The Aldrich, the Hay and the Pettenkoffer tests* are of help in measuring retained bile acid, as is the quantitative serum bilirubin test for measuring retained bile pigment, but are of little use in differentiating the nature of the liver disease. *Widal's hemoclastic shock test*, in this country, has not been of much help. No one test is capable of measuring all liver function, but when combined do help us to better differentiate and classify.

Cholecystography has its best use in diagnosing chronic cholecystitis, gall stones, and certain neoplasms of the gall bladder as we have already pointed out. The use of decholin-sodium in cholecystography—an improvement in technique recently introduced—materially enhances the value of this test because it measures the distensibility of the wall of the gall bladder in addition to its mucosal concentrating ability and its emptying power. A deficient shadow density, a loss of concentrating ability, and delayed emptying is highly suggestive. An absent shadow, except when due to cystic duct catarrh, is even more so. Demonstration of "positive" or "negative" stone shadows clinches the diagnosis of gall stones. Negative shadows of cholesterin stones should be differentiated from those caused by neoplastic growths, chiefly papillomas and adenomas. Irregularity in the outline of the gall bladder on cholecystography suggests adhesions and sometimes cancer. Thus cholecystography is of far greater value in chronic or advanced gall bladder disease but it is not within the scope of the test to pick up the early lesions of gall bladder disease so readily as will biliary drainage evidence. The two methods should supplement one another and the final diagnosis critically surveyed when discrepancies occur.

The most accurate results with cholecystographic diagnosis are obtained by the intravenous method. The oral method—although the more convenient—is too often fraught with uncertainties in locating or reading the gall bladder shadow because of gas shadows in the hepatic flexure. The technique of this useful test requires improvement in order to overcome this difficulty, but some one will overcome it.

Recognizing the early gall stone case, with preserved gall bladder function, without much damage to the wall, and with patent cystic duct is the most difficult one met with in cholecystography. Here "potential" stones may be present—the sand or minute gravel stage—and may not be visible and the diagnosis is best made by positive evidence in bile microscopy. A marked excess of cholesterin

or of calcium bilirubinate crystals is very suggestive and a combination of the two is almost pathognomonic.

In addition, we should remember that if such microscopy yields an excess of bile stained pus cells it means inflammation. Bile-stained bacterial colonies mean infection. Typical gall bladder, tall columnar epithelial cells, arranged in clusters, rosettes, or fan-shape groups, if in excess, and especially if associated with the small, oval or polygonal cells just beneath the surface epithelium, means an irritated mucous membrane. Excess bile-stained mucus means catarrh. Thus the combined evidence in microscopy supplementing an appraisal of the physical and chemical characteristics of the bile, is of the highest importance in diagnosis. If the case is one of chronic cholecystitis in a patient who has suffered a number of recurring acute exacerbations, the repeated attacks may have already stripped the irritated mucous membrane of its lining cells so that few if any may be found. This should be borne in mind, but the other evidence in aggregate will usually be sufficient.

TREATMENT

As we have already indicated, the curative treatment for chronic cholecystitis is surgical, but preceded and followed by medical measures. We are convinced that prolonged duodenal tube treatment, combined with other non-surgical management is ill advised and unfair to both patient and surgeon. We are convinced that this method has been over-exploited by certain doctors, technicians and nurses who are not only over-enthusiastic but too often insufficiently informed and poorly trained. As a result they have tended to discredit a method which if properly used is of great value to many sick people. There will not be found in our earlier publications on this subject any recommendation for the use of non-surgical methods in the treatment of chronic cholecystitis with certain exceptions to which I shall later refer.

Although valueless in accomplishing an actual removal of chronic cholecystitic disease that can only be achieved by cholecystectomy, biliary drainage by duodenal tube is of value in preparing the patient for safer surgery—especially those patients with complications—cardio-vascular, hepatic or renal—and it is invaluable as one of the measures in post-operative management to make the patient stay well and to derive the greatest benefit from the surgical step.

It is of great value in the direct treatment of those diseases and disorders of the liver which are often the left-over conditions that create post-operative morbidity and, therefore, somewhat discredit, in the biased mind, most useful and justifiable surgical tactics. Hence our keen interest in advocating a more standardized method of management.

We must add, too, that it is of value in the recognition and particularly in the treatment of many diseases and disorders of the liver itself such as early cirrhosis, the "typhoid liver carrier" and the "ameba carrier," subacute and chronic hepatitis and cholangitis, provided the common duct is not irreducibly obstructed; in disorders such as hepatic-intestinal toxemia, biliary migraine, and epileptoid convulsions which closely mimic true epilepsy. It is of service, too, in the treatment of subacute yellow atrophy of the liver, of hemolytic jaundice with splenomegaly, of the acute or chronic stages of various liver poisonings such as arsephenamin, cinchopen, atophan and the like. Furthermore, it is of value in the associated management of pernicious anemia and of diabetes, and postoperatively in adynamic ileus, persistent nausea, vomiting, and hiccoughing. It is certainly worthy of trial in persistent hiccoughs, whether postoperative or idiopathic, if resistent to other measures. The reason for all this we have tried to set forth in various articles. We believe it should be more extensively tried in the toxemias of pregnancy, and, more cautiously, in certain renal diseases, complicated with chronic passive congestion of the liver from a laboring heart.

What explanation can be given as to why diseases of such varied character are genuinely benefited by duodenal tube treatment? Until our chemical studies of the bile are better developed, a truly scientific answer cannot be given. But there is much clinical evidence to suggest that in such patients there may be circulating toxins—bacterial and chemical—from the liver and intestines, the removal of which, by external drainage of bile and internal irrigation of the intestines by transduodenal enema or lavage, improves the patient to a conspicuous degree. If such toxins are not removed, further resorption of them occurs in the intestinal tract and thus a vicious circle is produced.

If this hypothesis is correct we should, therefore, remember that there must be a great difference between the therapeutic effectiveness of "external drainage" of bile containing toxic products and viable bacteria when removed from the body by the duodenal tube compared with "internal drainage" accomplished by drugs and, to a less extent, by diets. Especially may this be true when this principle of external drainage is applied to livers suspected of having reduced detoxifying and bactericidal function, and also livers known to have diminished secretory-excretory function.

Preparation for operation. Our first aim should be to keep down the immediate operative mortality to 5 per cent or less; to keep down the post-operative morbidity to 10 per cent or less; and, between the two, to keep the operating room or hospital period complications down to the minimum.

To achieve these things the operating surgeon selected should be experienced in upper right quadrant surgery. The field is not the one for either the beginner, the heavy-handed surgeon, or one not master of the anatomy of this abdominal zone. His assistants should also be capable, to assure judicious speed in getting in and out, and they should be especially careful in the use of retractors and sponges to avoid trauma to the liver, blood vessels, bile ducts and nerves and to avoid spreading infection.

Most patients who die from cholecystectomy, cystostomy, anastomoses or operation upon the ducts, die from liver shock, from hemorrhage, from transferred infection, from toxemia, assisted by poor anaesthesia, and, after return to ward or room, from avoidable complications such as bronchitis, pneumonia, carelessness in catheterization, care of the mouth and so on due to inexperience on the part of interne, nurse or orderly. These latter are equally the responsibilities of the surgeon and the physician in charge. Hence the importance, when possible, of selecting a class A surgeon and a class A hospital where good laboratory service and a good dietetic kitchen are also maintained. We do not assert that throughout the country this is always possible, but it is the ideal we should seek.

The immediate preoperative preparation. If time permits, the immediate preoperative preparation should consist of:

a. Removing or minimizing infection in mouth, teeth, gums, tonsils and naso-pharynx.
b. Detoxicating the patient by proper care of the bowels, and by cleansing the colon, and also detoxicating, as well as preparing the operative field, by gastro-duodenal lavage and biliary drainage one or more times during the preoperative week.
c. During this period laboratory examinations of the urine, function tests of the kidneys and liver by the dyes, and by blood chemistry and serology should be carried out for operative safety.

All of this can be done without overtiring the average patient. If, however, the patient is unusually sick and a poor operative risk, two or more weeks devoted to such preoperative care is the wiser judgment, electing the operation day when the patient reaches his clinically best point.

If there is jaundice, the coagulability of the blood should be increased by daily injections of parathormone

and calcium gluconate—1 cc. of the former, 10 cc. of a 10 per cent solution of the latter—to minimize table and post-operative hemorrhage. The experienced surgeon will not—unless his hand is forced—operate in the presence of a rising icterus index and a rising serum bilirubin curve. He will wait until they fall to nearly normal or reach a plateau level. Preoperative blood transfusions will often be of great aid in saving a patient's life.

If there are cardio-renal complications, a poor myocardium, casts, albumin, and nitrogen retention, treatment directed to improving them is undertaken during the preoperative week.

If the blood sugar is low—below 85 mg. per 100 cc.—a daily intravenous injection of 25 gms. of glucose should be given, the last one just before operation, and if necessary another injection before the patient leaves the operating room and while still under anaesthesia. Every experienced surgeon knows how important this is in preventing death from liver shock due to hypoglycemia and to loss of stored glycogen. Since most deaths from that cause unexpectedly occur between the third and sixth day, it is wise practice postoperatively to estimate the blood sugar each day for a week to see that it is maintained at 90 mg. or above, and especially so if the patient's condition is not entirely satisfactory.

The week before operation ample sleep should be secured for the patient and especially the night before operation. The latter can be excellently accomplished by one and a half grains of pentabarbital-sodium or by three grains of sodium amytal or similar hypnotic. The operation preferably should be scheduled for the early morning or forenoon hours, so that the patient is spared several hours of wakeful nervous apprehension. Thus, before the hypnotic has worn off, the patient may receive the usual preoperative narcotic—one-fourth grain morphine—and go to the operating table blissfully indifferent. In the high-strung patient so much more susceptible, it would seem, to operative shock, experience proves that this is of the greatest importance to everyone concerned.

So, too, the anaesthetist should be carefully chosen and the anaesthetic likewise. Chloroform should never be used; ether as rarely as possible and in the least quantity. With the preliminary narcosis, a good anaesthetist can carry a patient through with gas-oxygen alone or supplementing avertin given by rectum. A well given spinal anaesthesia with spinocaine or similar synthetic drug has great advantages in producing a flaccid abdomen easier for the surgeon to expose the gall bladder because he does not have to pack away and thus traumatize the peristaltically active intestines. But it is not the method of choice for the highly nervous patient or for the clumsy, inexperienced anaesthetist. All methods of anaesthesia, however, are preferable to the older ones with chloroform or large amounts of ether, because they reduce post-operative nausea, retching and vomiting, thus sparing the patient much pain from unnecessarily wrenched abdominal muscles, and from the danger of setting up fresh internal oozing or dislocating drains, if they have to be used.

Any high-strung patient who has gone through such an operation even under the best conditions, as the author has done, knows that it is no Sunday School picnic, but may often, for the first few days thereafter, be a personally conducted tour through Hell. We have many times thought that there might be greater attention paid to many of these important details if every surgeon had himself been cholecystectomized. But we are not proposing this as a new order of things, for we know it would be promptly "killed in committee."

The operation itself. Neither shall we discuss the actual operating details, because it is not within our province to do so. But as a frequent operating-tableside observer we would generalize somewhat as follows. The liver should be kept warm by hot packs or by diathermy. The reciprocal dangers between a cold liver and a hot brain has been pointed out.

We prefer to see the gall bladder dissected free of its peritoneal attachments from the cystic duct upwards: the cystic duct tied off at a mid-position, not too high, but certainly avoiding injury to the common duct; an over-sewing of the peritoneal coats in the bed of the removed gall gladder and an avoidance of drains when possible. A cleanly resected gall bladder is the first step in avoiding morbidity. So many times, because of late pathology, a gall bladder bound down in adhesions, stones in vesicle and in ducts, and land marks obliterated, will grievously handicap the skilful efforts of the best surgeon. For this he can, in many instances, rightfully blame his medical confrère for dilatory negligence. Better team play should be developed between surgeon, internist and laboratory.

If the gall bladder contains stones or if the clinical picture was that of biliary colic, careful exploration of the cystic and common ducts for calculi should be made. The time to remove duct calculi is at primary and not secondary operation. The technique of how best to remove them we leave to the surgeon, for there are many disputed points regarding it.

If the common duct has been injured by disease or at operation, that is the time for choledochostomy, if the patient can stand it, and not at secondary operation, which is always more difficult. Or the surgeon may elect a cholecystogastrostomy or duodenostomy, (in our judgment the latter being preferable), but he should *never* do this operation unless he is *certain* that the cystic duct is patent, otherwise it accomplishes no good. This is the operation of choice in cancer of the common duct or of the pancreas. In the jaundiced patient, the experienced surgeon will see that he does not decompress the liver too rapidly or the patient will die of cholemia and liver shock.

Some surgeons hesitate to remove the gall bladder thinking they may need it later on for an anastomosis operation if the common duct should be injured. But after all is said and done, bold surgery by the experienced surgeon is best, whereas even conservative surgery by the inexperienced surgeon is serious, and in certain instances little short of unpremediated but legalized murder. We—and we are sure that you too—have such a high regard and profound respect for the accomplishments of the surgical artist that we hate to see his great achievements marred by the disasters of the surgical apprentice.

A statement as bald and frank as this should require some explanation. Any doctor after graduation and after admittance to State licensure legally is entitled to operate where and how he will. Simple surgery is one thing: gall tract, radical gastric and colon, renal, pelvic, brain or neurological surgery is quite another. The majority of us can do simple surgery without too much risk to a patient's life but we cannot do the difficult type. The master teachers of surgery, as heard and seen in their clinic amphitheaters, too often make the technique of delicate surgery seem too easy. It is true, of course, that in rural districts the courageous general practitioner *must* use the scalpel in cases urgently requiring surgery. It is also true that young surgeons *must* learn how to replace the masters of their craft. But we hold the view that it should be the incumbent duty of the teachers of surgery to tell their students, without braggadocio, but in fairness to the public, that certain types of surgery are truly difficult; to restrain the overenthusiasm of the novice to attempt them too soon, and to bring him along slowly to a mastership of his art. Until then, the large mortality and the appallingly high morbidity will continue. The published

statistics misrepresent the case. As high as they are in the aggregate, or as low as stated in selected series, they would be doubled if the rural surgeon operating under difficulties, or the overambitious novice operating in good hospitals would publish his results. It is our belief that the American College of Surgeons is fully aware of this situation and has taken or is taking steps to correct it.

In all cases with uninjured and patent common duct, but with damaged liver, we feel it most unwise and unnecessary to do surgical choledochostomy because in such cases drainage of the ducts and liver can be accomplished by the duodenal tube with greater safety and equal or greater efficiency. We have offered this view on several previous occasions and feel that here, too, better team work between surgeon and internist would yield better results.

Recently there has been in certain sections some tendency to return to the so-called "ideal operation" for calculous cholecystitis: to remove the stones and to drain the gall bladder or close it without drainage and to follow with duodenal tube drainage. However laudable the intent, and perhaps efficient in the isolated case, we doubt the wisdom of it. Too often the cystic duct is left obstructed and duodenal tube drainage of the gall bladder itself is therefore quite impossible. Furthermore, it is our belief that if there is sufficient reason to operate on the gall bladder there should be sufficient pathology to justify its removal. We fully agree with the surgeon who maintains that deep seated infection within the wall of the gall bladder cannot be cured by either surgical or medical drainage.

But let no man say that the physiology of the biliary system is not disturbed by removal of the gall bladder, for it most profoundly is. But nature and time and efficient post-operative management will usually bring it to a stage of compensation. Certainly the removal of a diseased gall bladder is the first essential step in relieving or curing a diseased liver, and the second essential step is the follow-up with duodenal tube drainage, appropriate dietetics, and appropriate chemo-therapy and in conclusion, we will briefly discuss this important phase of the subject.

The post-operative management. If team play between surgeon and internist has not already begun, it should certainly begin at this point. During the first ten days to two weeks the surgeon should be captain of the team, the physician acting only as friendly adviser when requested, but his presence is often helpful to the patient in bucking up the *morale* since usually he has known the patient longer and he or she relies on him "to look after his or her interests". But the physician should never use tactics that interfere with good team-play. If difficulties arise because the patient is doing badly the services of an experienced consultant may be very well worthwhile.

During the first few days opiates or narcotics should be pushed to keep the patient pain-free, mentally and physically relaxed and to allay nervous tension. A shocked nervous system may accelerate liver shock and always prolongs post-operative morbidity. Morphine is best, but if not tolerated, heroin is best. If heroin is not tolerated, a switch to hypnotics and sedatives should be made and given in sufficient doses. If blood sugar drops below 90 mg. to daily tests, glucose by vein should be given to keep the level to 100 mg. or even more. Fluid by mouth, if the stomach is tolerant, may be begun eight to twelve hours after operation, at first hot water, (or ice) one ounce each hour, increasing an ounce each time after three or four hours. The mouth should be kept very clean. In twenty-four hours, liquid foods may be begun and continued for at least seventy-two hours. Spoonfuls of cold junket or water-ice or not too rich ice cream are most gratefully received.

Water metabolism should be balanced by keeping intake and out-put charts. If needed, sugar, salt and soda bicarbonate may be added by proctoclysis, or salt and fluid by hypodermoclysis. With poor cardiac action and slowed renal excretion, sometimes pushing fluids by bowel, skin, and vein, will so water-log a failing heart and circulation as to lead to chronic passive congestion, pulmonary edema and death. We have seen this unhappy ending too frequently occur in our overzealousness to pull the patient through a stormy period, and therefore emphasize the need of cautious good judgment.

The patient should be kept warm, and warmth over the liver region is particularly useful.

The rectal tube should be used early for lower abdominal gas pains and a small normal saline or asafetida enema may be given on the second or third day.

For the relief of post-operative nausea, vomiting and upper abdominal painful distension (stomach and higher levels of small intestine), due to adynamic or paralytic inhibition, there is no measure more effective than gastro-duodenal lavage and aspiration of toxic gases and fluids. This may be accomplished by an inlying duodenal tube, introduced either via nares or pharynx as most comfortable to the patient. Rarely does it have to be continued longer than the fifth day. We reported on its value in this connection many years ago, and Jutte and Einhorn before us. More recently Wagensteen and his collaborators have introduced an improved technique of nasal catheter suction siphonage, using Levin's catheter tipped nasal-duodenal tube. Many lives have already been saved by its use post-surgically and otherwise. It is a method which can be endorsed and should become a part of standardized post-operative care in all abdominal operations. Hugh Young has reported on its value following urological surgery.

Furthermore, we have found that in some cases with paralytic inhibition of the intestines that peristalsis may be reëstablished by introducing into the rectum four to six ounces of filtered bile recovered from the duodenum, diluted with an equal amount of normal salt solution. The colon seems "hungry" for bile which fails to reach it because of faulty peristalsis; seems to absorb it greedily and completely, and in a number of cases shortly thereafter peristaltic *tinnitus* can be heard, gas is passed and a critical condition is turned for the better.

Another method worthy of trial is that of Ravdin and others: namely an intravenous injection of hypertonic salt solution—50 cc. of 8 per cent solution of sodium chloride is prepared by sterlizing in the autoclave at fifteen pounds pressure for twenty minutes. This is injected intravenously, very slowly, 2 c.c. to the minute. With a stethoscope over the abdomen peristalsis may often be noted before the conclusion of the full injection.

While waiting for the preparation of the hypertonic saline, one ampule of pitressen may be injected subcutaneously and repeated every two hours. Obviously too great delay in instituting any of the above measures allows a patient to reach a moribund stage when all measures are useless.

Avoid catheterizing, if possible. Once begun it may have to be continued for some days. Encourage the patients to void by all suitable measures during the first eighteen to twenty-four hour period. Once they have voluntarily voided their self-esteem is raised and their confidence restored.

On the fourth or fifth day after operation, small amounts of soft food may be added, but thereafter go slowly in resuming full trays no matter how hungry the patient may be.

We are strongly opposed to the patient resuming "house diet" so often in a week's time, and to hear the thoughtless remark of a foolish surgeon when he says "I have cut out your disease. From now on you may eat what you please". Some cases may get away with it by good luck,

but more often it is a responsible factor in producing post-operative morbidity and for weeks or months thereafter the patient complains of indigestion or abdominal distress that psychologically at least, may nullify the good effects of a technically well done operation. It takes time to re-establish physiologically satisfactory gastro-intestinal and biliary tract function. Especially is this delayed if the case has been complicated by gastro-duodenal or entero-colon disabilities or disease. The colon may be particularly troublesome for sometime after gall tract surgery.

We think it is a mistake to hurry the patient out of bed on the 6th to 8th day or out of the hospital on the 10th to 14th day no matter how well he may do. Breaking records or being a so-called "star patient" often proves a boomerang in subsequent months. We urge our patients to stay in the hospital a minimum of twenty-one days and in some cases even four weeks is none too long. Once returned to the home and away from the orderly routine and discipline of the hospital it is harder for them to maintain temperate restraint.

Unless the patient is critcially ill, we do not permit visitors during the first week, except perhaps one member of the family who is thoroughly *persona grata* to the patient, and then only for short periods to sit quietly and lend comfort and contentment by his or her presence. Many patients immediately recovering from an operative ordeal are so glad to find themselves alive and to "hear the birdies sing" that they are falsely buoyed up, "going on their nerve", and unrestricted visitors accelerate the inevitable let down that follows and retards progress. To one who has not undergone major abdominal surgery, and especially surgery near the region of the solar plexus, it may not be realized that there is always some shock to the nervous system.

Too many flowers in the room is bad practice. They absorb much oxygen needed for the patient and their care takes too much of the nurse's time that should be devoted to other duties. Of course this applies to the first week only or until after the patient is out of danger. Thereafter flowers, books and visitors do buck up the patient and relieve the monotonous hours of hospital life. Often ward patients do better than private patients perhaps because of ward restrictions, and therefore the foregoing remarks are pertinent.

The standard follow-up management. When the patient leaves the hospital, except for reporting to the surgeon for final inspection of scar and final dressings if any, the physician should assume the team captaincy. He should be chiefly responsible for instructing the patient in the appropriate follow-up program that will prevent or militate post-operative morbidity and guard against a flare-up of hepatitis or cholangitis so often unsuspected unless the duodenal tube is used to reveal it. In six to ten weeks after operation a control biliary drainage study, liver function tests and blood chemistry, should be done to make sure there is no residual catarrh, inflammation or infection. If this is present a few duodenal treatments, supplemented by one of the better bile salt or bile acid derivatives, will in a month's time usually clear up the condition. We cannot speak too forcibly of the wisdom of this because it does more than any single thing to prevent the need of a second operation. We have scores of history protocols that substantiate this.

The diet should be stepped up very gradually from a simple sensible one to a generous average dietary. But the patient should be particularly instructed that without a gall bladder he does not require quite so liberal an amount of the fats as theretofore. When the liver comes back to health and full functional capacity, and has compensated for the absence of the gall bladder, most patients can eat what and as they wish with ordinary prudence. But it is well to instruct the patient that a high carbohydrate diet protects the liver, if it has been damaged, and a heavy protein diet harms it.

The patient with uncomplicated chronic cholecystitis should be instructed to report to the physician once a month for the first three months after hospital discharge and thereafter every three months for the first year to detect and correct any morbidity that may occur, and to be coached in methods of prevention. The patient with chronic cholecystitis complicated by known liver disease, cirrhosis, hepato-cholangitis and toxic dysfunction should report oftener and be instructed how he must lead a "liver life" in the same manner as we instruct the diabetic, pernicious anemic or tuberculous patient how he must modify his living to get well and to stay well. In addition such patients will be greatly benefited by repeated short courses of biliary drainage which do more directly to help the liver revivify than does chemo-therapy. Regarding the latter, a calomel course once a month and the selection of a non-toxic bile salt or acid for interval use are the best.

The time to treat cirrhosis of the liver is in the early latent or compensated stage and the terminal decompensated stage with ascites may be prevented. We have many such cases whose disease has been kept controlled for fifteen years or more and paracentesis, the ammonia salts, and the mercurials, novasural and salyrgan, have not been required. All patients with known liver disease should temper their food, drink no alcohol, guard against a thyrotoxicosis and lead an outdoor life. They should be particularly warned against the use of the arsenicals, and the quinoline derivatives, such as atophan, cinchophen, farastan and the like.

Earlier in this paper we mentioned certain exceptions to the rule that chronic cholecystitis always demands surgery. There is not time to dwell on this. We have found that when a patient with calculous or non-calculous chronic cholecystitis is an elderly patient with an expectancy of life of ten years or less, is greatly enfeebled, or has a poor myocardium or coronary disease, or severe liver, renal, pulmonary or blood disease, the operative risk is often so great as to presage a table or hospital death which does no good to either patient or doctor and makes the undertaker the chief beneficiary. Under such conditions we proceed to prepare the patient as if for operation, but if he does well on a non-surgical program we extend it indefinitely, relying chiefly on the aid secured by duodenal tube biliary drainage which in these cases is less lethal than the knife. This may be criticized as poor policy in some cases, but we can now point to several score of elderly patients whose attacks of pain were arrested and who lived out or are living out their natural lives in comparative comfort. In cardiac cases the duodenal tube should be used with greatest caution and with an abbreviated technique and by an expert.

These are the occasional individual exceptions but on the other hand we should never forget Kehr's admonition of thirty-five years ago when he wrote "no one has it more in his power to increase the fame of surgical ability and science than the practising physician as soon as he early makes correct diagnoses and, when not too late, turns over his gall stone cases to the aseptic scalpel of the surgeon".

After the foregoing condensed review of this subject the author is sure that many will feel that we should adopt a more standardized method of management. Some may counter with the question, "Haven't we already such a standardized plan?" To them let us reply "Well, what of it? If we develop good team play and all work together we can improve it still further".

GASTRIC ULCERS ASSOCIATED WITH CINCHOPHEN POISONING*

REPORT OF AN INSTANCE WITH CONSIDERATION OF THE POSSIBLE ETIOLOGIC RELATIONSHIP

By
LEON BLOCH, M.D.
and
DAVID H. ROSENBERG, M.D.
CHICAGO, ILLINOIS

GASTROINTESTINAL symptoms, although commonly occurring in patients with cinchophen poisoning, have in most instances been attributed to clinical or to subclinical hepatitis. Rarely, have lesions in the gastrointestinal tract been recorded.

In 1932, Van Wagoner and Churchill[1] reported the finding of typical, chronic gastric and duodenal ulcers in 80 per cent of a series of 24 dogs which had received from 1 to 27 times the normal human kilogram dose of cinchophen. Of 7 dogs receiving the average human kilogram dose, it is significant that ulcers were found in 4. An optimum dose of 5 to 10 times the normal human dose was followed by ulcers in approximately 100 per cent. More recently, Barbour and Fisk,[2] in a study of the relationship between cinchophen and liver damage, noted gastric or duodenal ulcers in 4 out of 8 dogs to which large doses of cinchophen had been administered for three or more days.

Experimental observations of the above type must indeed awaken considerable interest in the finding of peptic ulcers associated with cinchophen poisoning in man. A careful search of the literature revealed but one such case, reported by Reah[3] in 1932. In this instance, the possible relationship of the gastric ulcer to cinchophen intoxication apparently received no consideration. An abstract of his report is therefore included here, viz.:

> A stevedore, aged 63, was first admitted to St. George in-the-East Hospital for the treatment of acute gout. *Mist. colchici* was prescribed, and later 7½ grains of cinchophen four times daily was added for two days. Thirteen weeks later he developed a sudden attack of lower abdominal pain followed by vomiting. The pain doubled him up and made him sweat and feel faint. Though less intense, the pain recurred during the next two weeks; it was worse after meals and during the night. Vomiting afforded some relief at first, as did bismuth tablets, but later it was ineffective. Ten days after the onset of pain, jaundice and light colored stools were noted. The jaundice became progressively more intense and he was admitted to the London Hospital four days later. There was no history of similar attacks nor of any indigestion. He had been a heavy drinker prior to one year before admission, but had imbibed very moderately since. In the past six months the patient had lost 14 pounds in weight.
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> *Physical examination* revealed tophi on the fingers and left ear. He was deeply jaundiced, the abdomen was distended, and there was tenderness in the right hypochondrium. The liver was four inches below the costal margin. The urine was deeply bile-stained. Roentgenologically, an ulcer was noted on the lesser curvature of the stomach. Blood pressure was 160/100. The patient became gradually worse, finally lapsing into coma. Four days before death, the blood urea was 37 mgm. per 100 c.c. He expired 16 days after admission.
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> *Necropsy:*—The liver was small and nodular and showed extensive destruction of the parenchyma with some regeneration. The stomach presented a peptic ulcer 1.5x1.8x0.24 cm. on the lesser curvature, midway between the pylorus and the cardia. There were many very shallow erosions along the greater curvature and streaks of altered blood in the stomach and in the jejunum. Microscopically, the peptic ulcer was shallow and crater-form. It had passed through the muscularis and was bounded by a narrow zone of dense fibrous tissue which extended for some distance along the submucosa and subserosa. An artery opened upon the surface, and a large artery in the base showed advanced endarteritis.

It is the purpose of our communication to place on record another case of cinchophen poisoning accompanied by gastric ulcers, and to direct attention to the clinical significance of this complication.

CASE REPORT

M.B., a white female, aged 69, entered the Michael Reese Hospital, February 27, 1932, for the treatment of a deforming polyarthritis of 5 years' duration. Over a long period during 1928 and 1930, she had received weekly injections of vaccine (type not known), and, for five months, dating from November, 1931, injections of Crowe's vaccine were given. About two years ago, she also had received several injections of a foreign protein; shortly afterward she began to take 0.5 to 1.0 gm. of "farastan" (mono-iodocinchophen) three times daily for a period of two to three months, with short intervening rest intervals.

Six months after starting "farastan", nausea and anorexia appeared, subsiding when the drug was discontinued. Thereafter and until the present hospital admission, she persisted in taking this drug for two to three days at a time, discontinuing it temporarily because of the nausea. For three weeks after leaving the hospital (April, 1932) she complained of generalized abdominal cramps, more marked in the lower abdomen, and associated with constipation. Despite warnings to the contrary, she continued to take "farastan" off and on until September, 1932. Persistent nausea appeared February 7, 1933, followed two days later by a profuse hematemesis. Seven hours later she had another hematemesis and died shortly afterward.

Necropsy Report: The body is that of a well-developed, well-nourished, white, adult female. The sclerae are clear. The joints of all fingers and of both knees are enlarged.

The liver is small, firm, light yellowish-brown in color and roughly nodular, and weighed 1250 gm. On section, the normal architecture has entirely disappeared, being replaced by irregular nodular areas in some places light yellowish-brown and in other places yellowish-pink in color. The gall-bladder and bile ducts are normal.

At the junction of the esophagus and the stomach, there is an old, irregularly outlined, longitudinal, ulcerating area 3 cm. in its greatest diameter. Its edges are firm and slightly elevated, and its base is smooth and pink-gray. It is attached to the outer layers of the stomach and esophagus. Three centimeters below the junction of the stomach and the esophagus, there is another longtitudinal ulcer measuring 3.5 cm. in its greatest diameter. The edges are raised, firm and undermined, and the base of the ulcer is pinkish-gray and slightly granular and exhibits many hemorrhagic areas. In close proximity to this ulcer, there are several small healed ulcers. There are many large varicose veins beneath the mucosa of the cardiac end of the stomach. In the first portion of the duodenum there is

*From the Departments of Medicine and Pathology, Michael Reese Hospital, Chicago, Illinois.

1. Van Wagoner, F. H., and Churchill, T. P.: Production of Gastric and Duodenal Ulcers in Experimental Cinchophen Poisoning of Dogs: *Arch. Path.* 14: 860: (Dec.) 1932. Churchill, T. P., and Van Wagoner, F. H.: Cinchophen Poisoning, *Proc. Soc. Exper. Biol. and Med.* 28: 581: (March) 1931.

2. Barbour, H. G., and Fisk, M. E.: Liver Damage in Dogs and Rats after Repeated Oral Administration of Cinchophen, Ethyl Ester of Paramethylphenylcinchoninic Acid (Tolysin) and Sodium Salicylate, *J. Pharm. and Exper. Therap.* 48: 341: (July) 1933.

3. Reah, T. G.: Cinchophen Poisoning, *Lancet* 2: 504: (Sept. 3), 1932.

considerable bright red blood. In the more distal portion of the small intestine and in the colon, bluish-black blood is mixed with the fecal material. *Microscopically*, the ulcers are shown to be lined by a dense, hyaline granulation-tissue which extends to the muscularis; there is a lymphocytic infiltration of all the layers of the stomach wall. (Fig. 1.)

Anatomic Diagnosis: Chronic gastric ulcers with chronic gastritis; healed ulcers in the region of the cardia; recent hemorrhagic erosions of the stomach; early toxic cirrhosis of the liver, marked cloudy swelling of the kidneys associated with arteriosclerotic scars.

DISCUSSION

The finding of peptic ulcers in only two patients who had been poisoned by cinchophen represents, at the present writing, a rare addition to the pathologic changes customarily observed in man at necropsy. More precise deductions relative to the frequency of ulcers are precluded by the fact that, of the fifty-three autopsy protocols which we reviewed, many contained no record of the condition of the stomach or of the duodenum.

The estimated presence of peptic ulcers in from 5 to 10 per cent of the general population of the United States offers interesting speculation concerning the etiologic rôle assumed by cinchophen and the part played by the factor of coincidence. Obviously, no decisive conclusion can be reached from the study of only two human cases, but certain points pertaining to a possible cinchophen etiology of peptic ulcer are worthy of consideration.

Experimental evidence, already reviewed, lends strong support to the theory of cinchophen ulcers, for cinchophen, given in normal, human, kilogram dosage over periods varying from 56 to 101 days, produced chronic peptic ulcers in 4 out of 7 dogs.[1]

Clinically, while we are cognizant of the fact that "silent" ulcers may have been preëxistent in both patients cited above, it is of interest, and perhaps suggestive, that no abdominal symptoms had become manifest before cinchophen was exhibited. In Reah's patient, intense abdominal symptoms, related to meals, appeared 15 weeks after the administration of 60 grains (4 gm.) of cinchophen, and were followed in ten days by the appearance of jaundice. In our patient, abdominal symptoms were not noted until iodocinchophen therapy had been in use for about six months.

From a study of the pathology of the ulcers, information of a suggestive nature may be acquired. Whereas typical peptic ulcers are usually round and whereas the great majority are distributed along the *"magenstrasse,"* it is noteworthy that the ulcers in our case were elongated, ovoid and quite irregular in contour and were found at the cardia and at the junction of the stomach and esophagus. The latter is a most exceptional location for peptic ulcer. Whether in Reah's case the advanced endarteritis* of the large artery at the base of the chronic gastric ulcer, by reducing the blood supply, provided a *locus minoris resistentiae* with the cinchophen acting as the provocative agent, or whether in our case the presence of healed and active gastric ulcers may be correlated with the intermittent ingestion of iodocinchophen, healing taking place during the rest periods, is purely conjectural.

The *mechanism of action of cinchophen* or *its derivatives* remains unknown. The most likely hypothesis, however, is that which recognizes the various toxic manifestations as allergic in nature, irrespective of whether these manifestations appear immediately after the first dose, after prolonged use of the drug or even some time after the drug has been discontinued. Such predisposing conditions as protein sensitization produced by previous protein or vaccine injections[4] (exemplified by our case); chronic infections; malnutrition which, as suggested in the preceding paragraph, may possibly include local malnutrition, as in Reah's ulcer with advanced endarteritis; cachexia; chronic alcoholism; or starvation are believed to render the individual susceptible to allergic reactions. Moreover, the intermittent administration of the cinchophens, especially iodocinchophen, is said to favor the development of an hypersensitive state (Quick).[5]

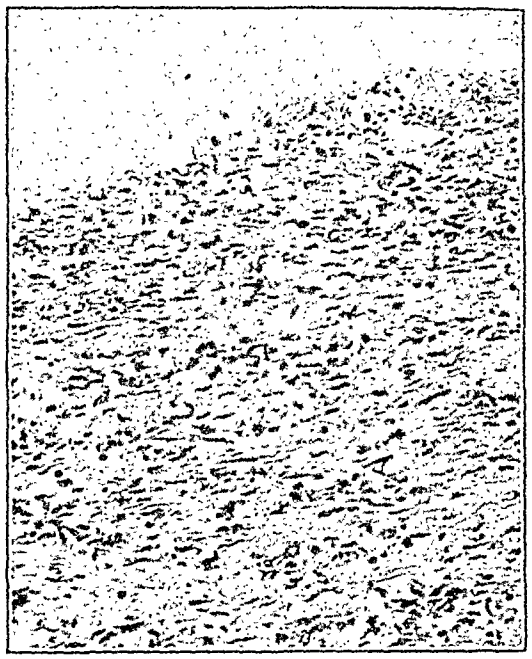


Fig. 1—Photomicrograph of the base of the chronic ulcer situated at the junction of the oesophagus and the cardia of the stomach, showing the absence of mucosa and its replacement by a dense granulation tissue infiltrated by lymphocytes.

Recently, Quick[5] suggested that acute yellow atrophy of the liver may represent a special form of the Arthus phenomenon. That a similar phenomenon may be at work in the production of cinchophen peptic ulcers is suggested by the experiments of Opie[6] and of Auer[7]. Extending Opie's work, Shapiro and Ivy[8] produced acute ulcers by the injection of specific antigen into the gastric submucosa of specifically sensitized dogs and rabbits. Auer hypothesized that it is unnecessary to inject specific antigen locally in order to effect a local anaphylactic reaction. If the specific antigen is present in the general circulation of sensitized animals in subliminal amounts, a non-specific irritant, by producing a local inflammatory reaction, might increase the local antigen-content sufficiently to result in a necrosis of the inflamed tissues. In their experimental studies on peptic ulcer, Shapiro and Ivy[8] elicited evidence tending to substantiate this belief. From such, it appears that cinchophen may act as a non-specific irritant to the gastric mucosa of a sensitized patient and thus produce ulcers. Once developed, the chronicity of such ulcers may be determined by the continued ingestion or the sustained action of the drug, or perhaps by local secondary endarteritic changes.

Whether or not the etiologic relationship of cinchophen to ulcers in man ultimately will become established, there is sufficient evidence at the present time to consider it a possibility, if not a probability, and to warrant further clin-

*The endarteritis may have been secondary to the inflammatory process at the seat of the ulcer, and thereby may have contributed to the chronicity of the ulcer.

4. Rabinowitz, M. A.: Atrophy of the Liver Due to Cinchophen Preparations, *Jour. A. M. A.* 95: 1228; (Oct. 25), 1930.
5. Quick, A. J.: The Probable Allergic Nature of Cinchophen Poisoning. With Special Reference to the Arthus Phenomenon and with Precautions to be Followed in Cinchophen Administration, *Am. J. Med. Sc.* 187: 115; (Jan.) 1934.
6. Opie, E. L.: Inflammatory Reaction of the Immune Animal to Antigen and Its Relation to Antibodies. *J. Immunol* 9: 231; (July) 1924.
7. Auer, J.: Local Auto-inoculation of the Sensitized Organism with Foreign Protein as a Cause of Abnormal Reactions, *J. Exper. Med.* 32: 427; (Oct.) 1920.
8. Shapiro, P. F., and Ivy, A. C.: Gastric Ulcer. Experimental Production of Gastric Ulcer by Local Anaphylaxis, *Arch. Int. Med.* 38: 237; (Aug.) 1926.

ical study and observation, especially of those patients who present abdominal symptoms following the administration of cinchophen. It is urged that a roentgenologic search for peptic ulcers be made in this group of patients. That such a study may prove to be of more than academic concern and indeed of therapeutic value, is indicated by the fact that a massive hemorrhage from an ulcer may be either the direct or the contributory cause of death, as attested by the two cases under discussion. Finally, the ubiquitous usage of cinchophen or its derivatives for the relief of various algesias suggests the need of an enquiry into the history of all peptic ulcer patients relative to these therapeutic agents.

SUMMARY

An instance of cinchophen poisoning associated with gastric ulcers is reported and another case is collected from the literature. The probability of cinchophen acting as the etiologic agent is suggested and discussed. Attention is directed to the need of further clinical and roentgenologic studies of the stomach and duodenum of patients who exhibit cinchophen poisoning. It is suggested that a careful *anamnesis* in all peptic ulcer patients from the standpoint of cinchophen therapy might yield interesting data.

ABSTRACTS

ASHER, MAURICE AND KRAEMER, MANFRED.

"Amebiasis in Northern New Jersey." Am: J. Med. Sc., 186: 409-413, Sept., 1933.

The authors state that in examination of stools they have been able to demonstrate cysts only in patients suffering from dysentery and have seen no healthy carriers.

The symptoms of amebic dysentery are diarrhea and weakness. There is not much pain although there may be occasional colic. The stools are usually liquid, fecal in character and contain blood. The blood may be occult. The specimen should be examined as fresh as possible within a few hours after passage, preferably in a warm chamber in order to find living forms. If kept warm for some hours it may be overgrown by colon bacilli. In the cases of chronic diarrhea in which the living amebae commonly are not found in the stool, a diagnosis is most difficult and several examinations must be made at intervals.

Once the diagnosis is made, the majority of patients are promptly cured by 9 or more intramuscular injections of emetin hydrochlorid (½ to 1 grain). In the long-standing cases with atrophic changes in the bowel wall and stool showing much pus and other evidence of secondary infection, emetin hydrochlorid is not so effective. Manson-Bahr recommends emetin bismuth iodid in these cases in doses of 3 grains per day for 10 or 12 consecutive days. In association with emetin bismuth iodid, he gives each morning an enema of 2.5 per cent Yatren (iodin-oxyquinolin-sulphonic acid) in warm water (250 cc.) The authors have used this method in one case with disappearance of cysts from the stool. It was not so successful in another instance. A high-caloric, low-residue diet as devised by Bargen and Victor in the treatment of chronic colitis was prescribed, in the belief that placing the large bowel at rest aids in the healing of the lesions. In the treatment of carriers, Craig mentions the use of emetin bismuth iodid and yatren. These drugs require that the patient be kept in bed. He found acetarson (Stovarsol) in tablets of 0.25 gm. 3 times a day for 1 week and repeated for a second week after a week's rest was effective in banishing the cysts.

Five cases in New Jersey are reported in people "who did not go to the tropics, the tropics came to them" by way of imported fresh vegetables. "Many cases of amebic dysentery in the temperate zone result from eating uncooked contaminated vegetables."

O. K. T.

ROGERS, SIR LEONARD.

"Tropical liver, hepatitis and abscess." Practitioner, 131: 117-123 (August) 1933.

Emetine hydrochloride is most satisfactory in amebic hepatitis and is given subcutaneously or intramuscularly in 1 grain doses in adults once daily, up to a total of 12 to 15 grains only in one course, for fear of its cumulative action producing muscular paralysis of a troublesome nature.

In order to lessen the danger of a relapse it is, however, advisable to follow the course of emetine injections by the oral administration of 20 to 30 grains ipecacuanha, with 10 grains of tannic acid to counteract its nauseating effect, last thing at night, three hours after a light meal, for a week with a view of eliminating the causative E. histolytica from the lumen of the bowel; some prefer the more drastic emetine bismuth iodide in 1 grain doses three times a day for a week for the same purpose. Stovarsol in .4 grain doses once daily for a week is also of value. Alcohol should be strictly avoided by all subjects of amebic disease as it strongly predisposes to amebic hepatitis and liver abscess.

The diagnosis and treatment of amebic abscess of the liver is discussed and it is noted that amebic abscess of the spleen may also occur.

O. K. T.

MAGATH, T. B.

"Amebiasis." Proc. Staff Meetings Mayo Clinic, 8:703-705, November 22, 1933.

In order to diagnose approximately 100 per cent of infestation, one must examine at least six formed stools. The same effect will be obtained by examining three liquid stools. An excellent demonstration may be made by obtaining a smear from the base of an ulcer, through the proctoscope, for then one sees thousands of organisms in a small space. Magath has not found the culture method as satisfactory as direct examination of stools.

Magath points out that the cysts, which transmit the infection are relatively resistant. They may exist for as long as six months in water and may pass through the gastro-intestinal tract of the common house fly without injury. Chlorine, which is so generally used for the purification of water supplies is relatively ineffectual; it takes a hundred times as much chlorine to kill the cyst of the ameba as is used in water supplies. While the ameba in the motile stage is quite readily killed, it is possible to transmit the disease by means of these forms, but the passage must be direct. Both the cysts and the motile forms are readily killed by drying and by a temperature as high as 68 degrees C. for five minutes.

A. G. N.

BROWN, P. W.

"A Clinical Note on Amebiasis." Proc. Staff Meetings Mayo Clinic, 8:706-708, Nov. 22, 1933.

Brown believes it wise to concentrate the dose of emetine hydrochloride, especially if the patient is acutely ill, by giving 3 grains (0.2 gm.) in divided doses the first day, 2 grains (0.12 gm.) in divided doses the next, and 1 or 2 grains in divided doses the third day. Emetine may be given intravenously, but results are so prompt and satisfactory with subcutaneous injection that a more hazardous method does not seem to be needed.

Arsphenamine while efficient is expensive and takes several weeks for a course. Of the arsenicals, stovarsol and acetarsone have been discontinued because cases of peripheral neuritis developed. Treparsol has been used and with proper caution no serious difficulties have arisen. Carbarsone does not seem to be superior, if as effective, as treparsol. This later drug is prescribed in tablets of 0.25 gm. with each of the three meals, for four days, and repeated for two more such courses, allowing a ten day period of rest between courses. Administration of treparsol and of emetine is started at the same time. In resistant cases in which one hesitates to continue these drugs for extended treatment, an iodine containing drug is fairly efficient. Yatren (known also as anayodin, chiniofon, and quinoxyl) is given orally, 3 gm. in divided doses, daily for a week; this treatment is repeated after an interval of a week. Vioform is given orally, 0.75 gm. in divided doses daily for ten days. Both drugs may cause diarrhea and it may be necessary to decrease the daily dose.

Failure to persist in adequate and properly spaced treatment is responsible for failures. After a course of treatment stools are examined on three successive days. If negative, this test is repeated a month later and again after two or three months.

CHOPRA, R. N.

"Treatment of Chronic Intestinal Amebiasis with Carbarsone." Indian Med. Gaz., 68:315-319, June, 1933.

Carbarsone (4-carbameno-phenyl-arsinic acid) was prescribed in 31 patients suffering from chronic intestinal amebiasis and 23 were cured. The drug was given in doses of 0.25 gm. twice daily for 10 consecutive days in gelatine capsules by mouth. The patients were kept on ordinary diet and, except a saline purgative whenever required to relieve constipation, no other drug was given. Five or more negative examinations of the stools on different days after cessation of all treatment was the criterion of cure. Four additional patients left the hospital improved but before these tests could be made. Three of the four failures had the cystic form. Auto-vaccine given either preceding or along with carbarsone treatment brought about a cure in cases in which bacillary dysentery was associated with the amebic infection. In one case carbarsone failed, but extractum kurchi liquidum with liver extract was effective. In another, cure was effected by a course of emetine bismuthous iodide 2 grains daily for 10 days. No untoward symptoms occurred in the series and continuation of the drug beyond the 10 day period is being tried in patients who have shown improvement but not cure in this length of time.

M. E. S.

DOUGHERTY, MARK S., JR., AND LEGUIN, FRANCES.

"Amebiasis." Am. J. Nursing, 33:1019-1024, November, 1933.

The nursing care, in general parallels that followed in nursing typhoid fever. At times the patient may have fifteen or twenty stools a day and the proper care of the skin on the buttocks, back, and perineal area must be given special attention. This is particularly true in the severe case of amebic dysentery. The skin should be kept clean and dry and bland ointments may be used to lessen irritation. Accurate records of the number and character of stools should be kept and it is particularly important to note any unusual amount of blood in the stools. The diet plays an important role in the treatment and consists essentially in a nutritious, low-residue, well-balanced diet. At first the patient may have a poor appetite and may have a moderate or severe anemia. The tray should be attractive and the nurse should see that a proper amount of food is eaten.

The disposal of the excreta is one of the greatest responsibilities of the nurse. The technic used routinely in disposing of typhoid stools may be followed. Probably the surest and most effective way to dispose of the stools from patients with amebiasis is to see that these stools are burned. The thermal death point of the cysts is generally considered to be about 68 degrees C.

Also the preparation of the stool for laboratory examination is of importance. As the endamebae stop moving quickly on chilling, the stool should be collected in a warm container and placed in the hands of the laboratory technician for examination at once. The interval of time between the passing of the stool and the examination in the laboratory should not be more than from fifteen to thirty minutes. The convalescent care is concerned mainly with adequate feeding and maintaining the patient's morale.

M. E. S.

POINDEXTER, HELDRUS.

"The Puerto Rican Strain of Endameba Histolytica. Comparison of the Diagnostic Value of Direct Smear Examination and Cultivation with Pathogenicity Test." The Puerto Rico Journal of Pub. Health and Trop. Med., 9:31-36, Sept. 1933.

One complete stool examination of 564 individuals showed 12.4 per cent positive for E. histolytica and 46 per cent positive for E. coli. It is believed that the percentage of positives would have been increased by repeated examinations of stools from these same individuals at short intervals. While the percentage of positives for E. histolytica by direct smear examinations alone and by cultivation were essentially the same, the combined methods gave a slightly higher percentage. When only the cysts are present in the stool, it is easier for the less expert laboratorian to make a differential diagnosis of E. histolytica from a culture (after excystation) than from the direct smear examination alone. Cultural methods should be more generally used, not as substitutes for the direct method, but as a useful supplement.

The high carrier incidence in the island and a relatively low percentage of clinical cases of amebiasis, Poindexter explains partly on the basis of acquired immunity. He also believes that the dietary habits of most of the people of the Island which consist of high carbohydrate diet tend to decrease the activity of the endamebae without retarding their rate of development or interfering with the life cycle. Experimental work on kittens fed on a high carbohydrate diet tended to confirm this interpretation of his observations.

S. S. Mc.

REED, ALFRED C.

"Amebiasis—A Clinical Summary." Calif. and Western Med., 40:6-11 (January) 1934.

The incidence of amebiasis in California is reported as approximately 10 per cent of the population. A high rate noted among house wives seems important because of the primary method of transmission by food handlers.

In treatment clinical and laboratory evidence of hepatitis is carefully noted, and the use of arsenicals is closely guarded accordingly. Patients showing cysts, with little or no diarrhea or dysentery, are given a routine course of carbarsone orally. In the presence of motile forms, carbarsone is given rectally in addition. In cases where amebas persist, or as a primary treatment, vioform orally is given in 0.5 gram dosage twice daily for ten days. These courses are alternated or repeated, with intercurrent free periods of ten days for full drug excretion, according to persistence or reappearance of amebas in the stools. Resistant cases may receive, in addition, emetin hypodermically, in appropriate dosage. The author is doubtful as to the actual added benefit from this procedure, although emetin is the drug of choice in frank amebic hepatitis. Tannin preparations and bismuth subcarbonate are used in persistent diarrheas and dysenteries symptomatically, combined with belladonna where pain is excessive.

Dietary principles in severe resistant cases include high protein, smooth diets, with a minimum of starch. Calcium and vitamin contents are kept high by use of tribasic calcium phosphate, dicalcium phosphate, and vitamin concentrates, especially American wheat kernels and extract of brewer's yeast.

Resistant cases, and those with incurable infiltrations and chronic ulcerative colitis, may require surgical treatment, consisting of appendectomy, ileostomy, pararectal and other procedures. Autogenous stool vaccines are of value in some cases where secondary infection prevents cure. Protein shock is occasionally of use. Colon irrigations with bactericidal solutions such as acriflavine, are helpful for bacterial complications. We have found a few ounces of one per cent tannic acid of symptomatic help where rectal bleeding is prominent.

K. A. B.

BOECK, WILLIAM C.

"Amebic Invasion of Lymphoid Tissue and its Probable Clinical Significance." Ann. Int. Med., 6:1564-1547 (June) 1933.

From the results of cultivation of Endameba histolytica in kittens (1924 and 1925) Boeck finds that there are two fundamental kinds of amebic lesions: first, erosion-ulcers of the epithelium which may become deep and undermining in character, often secondarily invaded by bacteria; second, a localized abscess in lymph follicles, liver, lung, brain and spleen. (Pathological pictures are presented to illustrate these types.) His pathological observations, applied clinically, indicate that all patients in poor health and underweight, those with nervous and physical exhaustion, and those who may be subject to recurrent attacks of arthritis and other diseases commonly associated with focal infection, should be thoroughly examined for this parasite. In the so-called carrier cases of chronic amebiasis, slight erosion-lesions of the intestinal mucosa or invasion of solitary lymph follicles may represent portals of entry for the absorption of toxins from the colon. The bacterial toxins may be the more important etiologic factor in the production of ill-health and chronic disease in such cases of parasitic invasion.

Further investigations on patients with Hodgkins disease have failed to show any amebae present in the enlarged lymph nodes.

R. M.

Amebic dysentery, a review. J.A.M.A., 101:1639-1641, Nov. 18, 1933.

A review of the literature on the subject of amebic dysentery, covering symptoms, diagnosis, complications, prognosis and treatment, is presented as a summary of current knowledge regarding this disease.

J. T. S.

LUPO, MASSIMO.

"Un segno radiologico della colite da ameba istolitica (A radiologic sign of colitis due to Ameba histolytica)." Radiol. Med., 20:709-715, June, 1933.

The author presents radiograms in four cases of ameba histolitica illustrating a button-like niche, characteristic, he believes, of cases of ameba histolytica and one which he has never seen in any case of non-amebic colitis. The barium outlining the deep ulcer undermining the mucosa of the intestines is the base of the collar button and this is connected with the bowel lumen by a short and small canal (the stem) and the ulcerated mucosa is the head of the collar button. The margins appear regular and plain, but observed with the lens are fringed and anfractuous.

W. H. R.

FITZGERALD, G. H.

"Gavano, a new specific for Amebic Dysentery." Indian Med. Gaz., 68:458-459 (August) 1933.

To what extent Gavano, a new synthetic preparation by Bayer, is capable of permanently eliminating the Entameba histolytica, the author cannot say as yet; but in no case in his experience has it failed to relieve the symptoms of amebic dysentery, and this without causing the patient any of the discomforts associated with any of the recognized forms of emetine treatment. Nausea is unknown.

Through its action on the medullary centers it causes a lowering of blood pressure and diminishes CO_2 elimination; this increases vagal activity and results in increased peristalsis of the large intestine.

B. S. H.

BARROW, JOHN V.

"Amebic dysentery." Calif. and Western Med., 40:6061 (January) 1934.

Emetin, as well as arsenic, should not be used beyond their physiologic activity. Emetin hydrochloride given intravenously, one-third grain, daily the first week, repeated on alternate days thereafter for five doses, will accomplish as much as the large dosage and practically insure against injury by the drug. The same dosage twice weekly may be continued for months, with no cumulative action. The liver is thus protected and there is less danger of relapse. Meanwhile the treatment with carbarsone should start co-incidentally with the emetin and be continued with one capsule each morning and evening, for ten days only. One should be constantly on guard against arsenical saturation, which is usually first manifested by redness or itching of the skin. The arsenical treatment may be repeated in full or in part, after a ten-day interval. One repetition usually suffices to rid the patient of tropozoites and cysts. Watchful search for organisms in the stools during the next year, at intervals of two or three months, is the safest protedure in guarding the patient against damage from the organism and from the drug. The author has never found a case of damaged heart in patients so treated.

J. R. B.

SUMERLIN, H. S.

"Amebiasis incidence in private practice." Jour. A.M.A. Feb. 3, 1934, 102: 363-364.

The incidence of Endamoeba histolytica varies from 0.2 to 15.58 per cent, depending, no doubt, upon the class of patients and the geographic location. Summerlin reports an incidence of 2.3 per cent in 1,339 adults and 0.4 per cent in 513 children examined in the Rees-Stealy clinic, San Diego, in the past four years. Routine examinations were made, not limited to patients with gastrointestinal complaints. Experience in this clinic shows that a single fecal examination will reveal the protozoa actually present in over 90 per cent of the cases, if a liquid specimen is collected following a saline cathartic and examined while warm.

For the detection and identification of protozoa, a combination of the cover-glass preparation in physiologic solution of sodium chloride and a modification of Donaldson's iodine-eosin mixture[1] was employed. With the iodine-eosin mixture properly adjusted, the cysts appear as bright yellow circles in a red field: the flagellates and motile amebas stain red. The oil immersion objective was used to study the internal structure. In almost every case the cysts of Endamoeba histolytica can be identified in the cover-glass saline solution preparation by their large highly refractile chromatoidal rods. The identification of motile forms is frequently difficult. Good illumination is absolutely essential. It was found unnecessary and undesirable to use permanent preparations stained with Haidenhain's iron-hematoxylin solution of sodium chloride saturated with iodine, 1 part: physiologic solution of sodium chloride, 2 parts. These solutions are kept in separate dropping bottles and mixed fresh daily.

J. H. A.

1. Saturated solution of eosin in physiologic solution of sodium chloride, 1 part; 5 per cent potassium iodide in physiologic solution of sodium chloride saturated with iodine, 1 part; physiologic solution of sodium chloride, 2 parts. These solutions are kept in separate dropping bottles and mixed fresh daily.

"Amebic dysentery and food handlers." Lancet, Jan. 6, 1934, pp. 46-47.

In the public health section of the Lancet, the Chicago epidemic is discussed and it is said:

"So far as public health control in England is concerned there is perhaps less likelihood of an outbreak here: but should one arise the means of checking it would be less effective than in Chicago. No distinction is made in our notification scheme between amebic and bacillary dysentery, nor are there powers available for the routine examination of food-handlers."

W. E. V.

ROCK, ROBERT E.

"Management of amebic dysentery." Minn. Med., 16:748-749, Dec., 1933.

Emetine is sometimes recommended in doses of 0.10 gm. (gr. 1½) daily for ten or more days. Rock warns that this invites depression and paralysis of the heart (shortness of breath and marked cardiac arrythmia) gastrointestinal irritation and acidosis. He recommends complete bed rest. Emetine hydrochloride should be given subcutaneously in daily dosage of 0.04 gm. (gr. ⅔) for seven days. Intramuscular injection of emetine is exceedingly beneficial; intravenous administration (0.03 gm. or gr. ½), used rarely in acute fulminating type, is inadvisable. Bismuth subnitrate or subcarbonate is very effective in large, heaping teaspoonful doses every four hours for 7 to 10 days. For the first few days the powder is given suspended in warm water, later in hot milk. The subnitrate is considered better treatment than the bismuth emetine iodide. Liquid diet, consisting of well-cooked vegetable soups, tea sweetened to the limit, etc., is recommended during the first 4 days of the acute stage. Ipecac in salol-coated pills is begun at the entrance to the convalescent stage with cyst-laden stools. Ten pills of 5 grains each, and with the salol covering pierced by a needle, are given at bedtime each night for one to two weeks. Rock also mentions yatren. It may be given by mouth (gr. VI t.i.d.) and concurrently by rectum (200 cc. 2.5 per cent retained for 2 hours) if indications point to lesions in the lower bowel. A cleansing enema of 2 per cent sodium bicarbonate precedes the yatren retention. For clearing up the histolytica carriers, nearsphenamine is given intravenously (0.3 gm.) every third day until ten injections are reached. Stovarsol or treparsol is given by mouth in doses of 0.25 gm. t.i.d., for a week; then once daily for 2 weeks. Complications will be lessened by a careful note of any fever rise or leukocytosis; thus a pre-suppurative hepatitis is found early. After becoming cyst-free, the patient should report every three months during the first year for stool examination.

D. F.

SAUNDERS, EDWARD WATTS, HOLSINGER, HUBERT B., AND COOPER, MARY A., B. S.

"The role of infection in gastric and duodenal ulcer." Am. J. Med. Sc., 187:246-248, Feb. 1934.

A streptococcus was isolated from 30 resected ulcers of the stomach and duodenum by planting bits of the ulcer tissue in 0.5 per cent hormone agar immediately upon resection. All these strains were proved identical by agglutination, cross agglutination and agglutinin absorption and also identical with three strains isolated from cow's milk. In previous work its non-relationship to all other focus streptococci was proved. Its further relationship to ulcer has been previously shown by the high titer agglutination of patient's sera suffering from gastric ulcer against an antigen of this organism, and the non-agglutination of control sera. It has been demonstrated to be present in great numbers in immediately prepared Levaditi sections of human ulcers. Experimental work was next undertaken to determine the role played by this organism in the production of ulcers. Following surgical duodenal drainage in dogs, 14 typical ulcers were found in 5 of the group of 10 fed cultures of the organism, and only 2 erosions in 2 of the control group of 9 not fed the organisms.

C. G. O. T.

SAUNDERS, EDWARD WATTS, HOLSINGER, HUBERT B., AND COOPER, MARY A., B. S.

"Anaphylactic-like reaction produced by the streptococcus of gastric ulcer." Am. J. Med. Sc., 187:249-253, Feb. 1934.

Further study to determine the tissue reaction of animals to the streptococcus isolated from gastric ulcer demonstrated that there is a definite animal reaction towards the organism (streptococcus and that this reaction can be made more severe by previously inoculating the animal with the organism, and that an immunity can be developed in the animal by frequent injections at daily intervals. This type of sensitivity which the animal develops may well explain the periodicity of symptoms presented by ulcer patients. It would also explain the local reaction which occurs when vaccine therapy is instituted.

C. G. O. T.

FONTAINE, RENE AND MARCEL BERARD.

"La section des nerfs erecteurs d'Eckard a-t-elle un effect durable sur la motilite de la vessie et du colon? (Does section of the erector nerve of Eckard have a lasting effect on the motility of the bladder and colon?)" Presse Med. Jan. 17, 1934, 81-84.

Adamson and Aird (Brit. J. Surg. Oct. 1932) produced megacolon in the cat by simple section of the erector nerve of Eckard, apparently contributing to the support of the neurogenic theory of the pathogenesis of megacolon. However, repeating these experiments in dogs, the authors observed merely temporary constipation and an incontinence of feces. At the end of a few weeks, they never found colon distention, and the cause of magacolon seems to them a more complex one. (The balance of the article is concerned with the physiology of the bladder.)

P. D. L.

GREGOIRE, RAYMOND.

"L'oesophagoplastie prethoracique dans les stenoses incurables de l'oesophage. (Prethoracic esophagoplasty in incurable stenosis of the esophagus.)" Presse Medicale, Jan. 27, 1934, 145-147.

A case of complete cicatricial stenosis of the esophagus is reported in which an artificial canal was successfully constructed and functioned satisfactorily. The new canal was formed of three parts: a crevical esophagus, a short segment, active and contractile; a long segment formed of skin, consequently inert; and a lower segment of variable length, formed of small intestine, active and contractile. After a short period in which to become accustomed to eating under the new conditions, the patient is able to eat what he pleases and as well as anyone with a normal esophagus.

P. D. L.

FELDMAN, MAURICE.

"The redundant duodenum." Am. J. Med. Sc. 186:198-202, August, 1933.

From a study of ten cases of redundant duodenum, it appears that the superior portion is the more frequent site and that ulceration is not an unusual finding in these cases. The clinical significance of the redundant duodenum has not been fully established. It is apparently more common than is ordinarily recognized. The Roentgenologic method of examination offers the best possible means of establishing the diagnosis.

PALMER, WALTER LINCOLN.

"Fundamental Difficulties in the Treatment of Peptic Ulcer." J. A. M. A., 101:1604-1607, Nov. 18, 1933.

Evidence is summarized, showing that ulcer formation depends on the presence of acid gastric juice. Treatment to be successful must protect the lesion or the cells of the mucosa from the destructive effect of the acid. The antacid regimen of Sippy or one of its modifications is, on the whole, the most satisfactory form of medical therapy now in use. Mucin or some such substance may form a coating over the surface of the ulcer and thereby protect it from the attack of the acid, but satisfactory proof of this has not yet been produced. Mucin does not accomplish complete neutralization of the gastric free acidity. Atropine, in physiologic doses, decreases gastric secretion, but the attendant atropine effects seriously limit its usefulness.

Gastro-enterostomy may or may not lower the acidity but rarely produces complete neutralization. Subtotal gastrectomy usually results in complete and permanent anacidity. The objections to its general adoption are the relatively high mortality rate and the gravity of the lesions when they do recur.

COMROE, BERNARD I.

"Association of pituitary tumor and peptic ulcer." Am. J. Med. Sc., 186:568-573, Oct., 1933.

Two cases are reported of primary pituitary tumor associated with peptic ulcer in which (for the first time, the author believes) the diagnosis was made before death. Cushing has recently called attention to the relationship between lesions of the interbrain and peptic ulcer. Inasmuch as lesions of the pituitary gland are always associated with disorders of the suprarenal cortex, and since recent experiments have shown that damage to the suprarenals will repeatedly produce intestinal ulcers (in animals), it is suggested that these two cases might supply the missing link in the chain of evidence supporting the alleged etiologic relationship between peptic ulcer and the endocrines. Treatment of early cases of peptic ulcer by means of pituitrin subcutaneously seems worthy of trial.

VANZANT, FRANCES R., ALVAREZ, WALTER C., BERKSON, JOSEPH, AND EUSTERMAN, GEORGE B.

"Changes in Gastric Acidity in Peptic Ulcer, Cholecystitis and Other Diseases." Arch. Int. Med., 52:616-631, October, 1933.

An increase in free acidity occurs in the case of duodenal ulcer (expressed as approximately 12 units), an increase which varied with the size of the ulcer, with the number found at operation and with the severity of the symptoms produced. Less than one per cent of the patients with duodenal ulcer failed to show free acid after an Ewald test meal. No difference was found in gastric acidity to indicate those cases in which, after gastroenterostomy there would be recurrence and those which would remain symptom free.

In 174 men with gastro-jejunal ulcer, the mean free acidity was lower than normal by about 4 units. The incidence of true achlorhydria was 71 per cent of normal. In the case of gastric ulcer the mean free acidity was lower than normal by about six units. This lowering was more marked in the cases of ulcers situated in the proximal two-thirds of the stomach. The incidence of achlorhydria was half of that observed in normal persons.

Practically no change from normal was found in the mean free acidity of patients with cholecystitis and cholelithiasis. No change from normal could be found in the gastric acidity of patients who had submitted to cholecystectomy. In the case of patients who suffered with a combination of disease of the gallbladder and ulcer of the duodenum, the acidity was slightly higher than in the case of patients with uncomplicated duodenal ulcer.

Normal standards had previously been established based on the records of 3,746 persons (Arch. Int. Med. 49:345, March, 1932). The author's technic is given in the previous article.

KING, E. S. J. AND P. MACCALLUM.

"Pancreatic Tissue in the Wall of the Stomach." Archiv. Surgery, 28:125-138, January, 1934.

Nodules of tissue indistinguishable microscopically from pancreas have been observed in the wall of the stomach by many investigators. From a study of four cases of pancreatic tissue in the wall of the stomach and a review of the literature it is concluded that pancreatic tissue arises from the epithelium of the stomach under the action of abnormal stimuli and does not arise as a "cell rest" from the displacement of a pancreatic anlage during embryonic life.

COLLINS, A. N. AND G. L. BERDEZ.

"Chyle Cysts of the Mesentery." Arch. Surg. 28:335-344, February, 1934.

A freely movable tumor in the lower part of the abdomen which fluctuates and has a midline attachment should suggest mesenteric cyst. The discovery of chylous ascites by exploratory puncture may assist in establishing a differential diagnosis. Marsupialization has resulted in the largest number of recoveries.

Chyle cysts of the mesentery are relatively rare but have been encountered from early childhood to old age. Two cases are here reported.

FINE, JACOB, AND LEVENSON, WALTER S.

"Effect of Foods on Postoperative Distention." Am. J. Surg., 21: 184-203, August, 1933.

It appears that in the treatment of distention, the baneful influence of certain foods must be considered along with the probably equally vital role of swallowed air. Liquid carbohydrates are a particularly important source of distending gases. The higher the glucose content of these carbohydrates the more gas is likely to form, although certain ones containing not more than five per cent glucose may also produce severe grades of distention. Of the latter, orange juice and ginger ale deserve special mention. Other foods capable of causing significant degrees of gaseous distention are milk, whether pure or in mixed form, and foods rich in cellulose, such as bean puree. The general condition of the animal subjected to the experiment, the amount of food, and the state of motor, secretory and absorptive activity in the intestine may vary the amount of distention even in the same type of operation and similar preoperative and postoperative management.

The necessity of administering liquids and carbohydrates in the immediate postoperative period can be met by the parenteral administration of glucose solutions, while the desirability of re-establishing normal peristalsis, which is better initiated by the resort to solid or semisolid foods, would be more safely and effectively accomplished by the use of such foods as toast, gruel or other cooked cereals, egg albumen and other non-gas producers within a reasonable time after nausea and vomiting have subsided.

RANKIN, FRED. W

"The Present-Day Treatment of Colonic Cancer." Am. J. Surg., 23:36-42, January, 1934.

Almost a year has elapsed before the average patient with cancer of the colon or rectum has an accurate diagnosis made, although diagnosis in the hands of efficient roentgenologists is so accurate as to leave little to be desired. There are no pathognomonic symptoms which bring individuals suffering with organic lesions of the large bowel to seek advice at an early period. Acute intestinal obstruction is rarely produced by colonic cancer so that preliminary preoperative preparation and careful selection of operative procedure is possible. Adequate decompression of the colon by means of irrigations and mild purgatives is first attempted. If such measures fail, surgical decompression is essential as a means to restore the normal healing power of the issues prior to anastomoses to prevent postoperative leakage. Feeding barium by mouth is deprecated because of obstruction produced and difficulty of removal. Rehabilitation of the patient is attempted in preoperative care. A diet high in calories and low in residue is utilized. For a number of years the author has used a mixed vaccine of streptococci and colon bacilli administered three days preoperatively. Theoretically this is a correct procedure and practically it has proved useful.

Discussing operative technic, the author believes that the graded operation is best in the majority of cases. The most essential general principle in the postoperative care is the prevention of peristaltic activity as nearly as possible; first, by adequate administration of morphine; second, by refusal to give fluids by mouth until after a postoperative period of forty-eight to sixty hours has past.

Other important factors in the author's treatment of these cases are discussed together with an analysis of end-results. An average of the five-year cures of cancer of the right bowel, with and without nodal involvement, showed 57.6 per cent, while the growths of the left half of the colon showed a total of 51.3 per cent of five-year cures.

BENEDICT, EDWARD B. AND ALLEN, ARTHUR W.

"Adenomatous Polypi of the Stomach, with Special Reference to Malignant Degeneration." Surg. Gynec. Obst., 58:79-84, January, 1934.

In a series of 17 cases of gastric polypi giving fairly severe symptoms, there was microscopic evidence of potential malignancy in seven cases, or an incidence of 41.2 per cent. In view of this high incidence of malignancy and the tendency to moderate or even very severe hemorrhage, radical surgery must be seriously considered in all gastric polyps.

Section II.

Experimental Physiology

Contributions by

STEWART G. BAXTER

SYMPATHETIC SECRETORY INNERVATION OF THE GASTRIC MUCOSA*

By

STEWART G. BAXTER

From the Department of Physiology, McGill University, Montreal, Canada

EXPERIMENTAL data concerning the influence of the sympathetic nervous system on the secretory activity of the stomach are scarce and controversial.

According to Bickel (1925) and his co-workers the fundic glands are innervated by both parasympathetic ("secretory") and sympathetic ("trophic") fibres which *excite*, and by sympathetic fibres which *inhibit* the secretory activity, while the pyloric portion of the stomach is innervated solely by sympathetic fibres, some of which excite, others of which inhibit secretion. Volborth and Kudriawzeff (1927), on the other hand, consider the sympathetic nerves as secretory nerves to the fundic glands. *B. A. McSwiney (personal communication to Dr. B. P.* Babkin) obtained a secretion of mucus from the isolated pyloric portion of the stomach during splanchnic stimulation. No less conflicting are the data concerning the effect of epinephrine on gastric secretion. Hess and Hundlach (1920), Rothlin (1920) and Moll and Flint (1928) reported an inhibition of the gastric secretion, whereas other investigators have demonstrated a secretory response of the gastric glands on administration of epinephrine (Yukawa, 1908; Loeper and Verpy, 1917; Lim, 1923; Ivy and McIlvain, 1923; Sirotinin, 1924). According to Bickel (1925) and his associates, epinephrine does not influence the secretion from a Pavlov or a Bickel pouch, but slightly increases the secretion from a Heidenhain pouch.

In view of this uncertain state of affairs, a fresh attempt has here been made to determine experimentally the function of the sympathetic nerve in relation to the secretory function of the gastric mucosa.

METHODS

Acute experiments were performed on dogs and cats. On the day preceding the experiment the animals were given only milk and water. Thus the stomach was free from food and usually in a quiescent state at the time of experiment. After a brief anaesthesia with ether, 0.5 g. urethane and 0.05 g. chloralose per kilo were introduced intravenously. The vagi were sectioned in the neck or below the diaphragm, or included in the subdiaphragmatic ligature of the oesophagus. The oesophagus and pylorus were always ligated. In most experiments the adrenal veins were ligated in order to avoid the secretion of epinephrine caused by splanchnic stimulation. A small metal fistula was inserted in the posterior wall of the stomach and brought out through a stab wound in the left flank.

The greater splanchnic nerves were tied, and in most experiments without being severed, placed in special shield electrodes, designed by A. H. Masters, mechanician of the Department of Physiology. The electrodes consisted of an ivory box about 6 cm. long and 0.5 cm. wide, which contained two embedded platinum electrode wires, 3 mm. apart. The wires were exposed in a small chamber at one end, just large enough to admit the splanchnic nerve easily. The chamber was covered by a T-shaped bar, which was operated by a small wire spring. This bar kept the nerve firmly in contact with the exposed portion of the wires and prevented other tissues from coming in contact with the exposed electrodes. In these electrodes the splanchnic nerves retained their excitability for 8 to 10 hours, i.e. much longer than in ordinary electrodes.

Rhythmic stimulation was employed, a metronome being used to break the circuit. The splanchnic nerves were stimulated alternately—five minutes' excitation and five minutes' rest. The blood pressure was registered as an index of splanchnic stimulation. Some experiments were also done in which a Palmer induction coil of low frequency (3 to 4 shocks per second) was employed.

The acidity of the gastric secretion was determined by titration with 0.01 N NaOH, Topfer's reagent and phenolphthalein being used as indicators. The alkalinity of the mucus samples was determined by back titration with 0.02 N HCl after 0.5 c.c. of the secretion had been boiled with 0.1 N NaOH. The total chlorides were estimated by the method of Wilson and Ball (1928), and the peptic power by Christiansen's modification of Mett's method (1912). The results were rendered comparable by the use of a standard of dog's gastric juice kept on ice. The reducing power of the gastric secretions was determined by the method of Webster and Komarov (1932).

EXPERIMENTAL RESULTS

Stimulation of freshly cut splanchnic nerves. Long-continued rhythmic stimulation of the splanchnic nerves

*A preliminary communication was published in the Proceedings of the Society for Experimental Biology and Medicine, 1932, vol. 29, p. 511.

TABLE I

Effect of splanchnic stimulation on the secretory function of the stomach: analysis of the secretion.

Exp. April 1, 1930.

Dog. 5.4 k. Oesophagus tied in neck; adrenal veins ligated; vagi sectioned in neck; both splanchnic nerves in shield electrodes; fistula in posterior wall of stomach; stomach reaction neutral; stimulation right and left splanchnic nerves alternately (5 minutes' stimulation and 5 minutes' rest).

Sample No.	*Time* min.	*Vol.* c.c.	*Alkalinity* mil. equiv.	*Total Cl* mg. %	*Reducing Power* mg. % glucose	*Peptic Power* Mett's units	*Total Solids* mg. %	*Org. Mat* mg. %	*Ash* mg. %	*B. P.* mm. Hg	*Remarks*
1	30										Control, no secretion.
2	60	4.5	13.6	447.0	161.5	6.25	2100	1180	920	38-46	Stimulation R. & L. splanchnic, coil 10 cm.—9 cm.
3	30	0.8								50	No stimulation.
4	60	3.5	14.0	479.0	146.0	16.0	1860	900	960	50-55	Stimulation R. & L., coil 9 cm.—8.5 cm.
5	60	3.5	11.6	499.0	124.5	36.0	1720	760	960	40-45	Stimulation R. & L., coil 8.5 cm.
6	60	3.0	11.2	501.0	108.0	16.0	1840	860	980	30-40	Stimulation R. & L., coil 8.25 cm.
7	60	3.0	13.6	462.0	112.0	16.0	1640	720	920	30-35	Stimulation R. & L., coil 8.0 cm.
8	30	0.5									No stimulation.
9	60	3.0	13.6	510.4	114.0	16.0	1500	580	920	26-32	Stimulation R. & L., coil 8 cm.

N. B.—At end of experiment whole stomach alkaline, surface covered with clear shiny mucus—more in pylorus than in fundus.

resulted in the secretion of a thick whitish mucus at a fairly even rate, not exceeding 3.5 to 4.0 c.c. per hour. Its reaction was usually alkaline, and its enzymatic power after acidification low. The concentration of organic material in the secretion progressively fell, whereas the mineral parts remained constant during the whole experiment. The reducing power of the secretion, expressed as per cent of glucose was fairly high, indicating probably a high content of mucoprotein. It diminished somewhat towards the end of the experiment. The Experiment of April 1 (Table I) is quoted as an example.

Although at the beginning of some experiments the reaction in the stomach was occasionally acid, during the stimulation of the splanchnic nerves it gradually became alkaline. No marked difference was noted in the volume of the secretion or its properties whether induction currents of high frequency (50 to 60 shocks per second) or low frequency (3 to 4 shocks per second) were applied to the nerves.

In a series of control experiments on animals prepared as described above but without nerve stimulation, the secretion during six to seven hours was at first acid and then alkaline, and was extremely scant (0.2 to 0.3 c.c. per hour). The high initial blood pressure observed in some experiments was unfavorable to the secretion of mucus.

Atropine did not markedly affect the volume of mucoid secretion produced by rhythmic stimulation of the splanchnics. Thus in the Experiment of July 15, on a dog of 7.8 kilos, control stimulation of the right and left splanchnics (coil 11.0 to 10.5 cm.) for 60 minutes gave 0.9 c.c. of mucoid secretion. After atropine (6 and 4 mg. intravenously) 30 minutes' stimulation of both splanchnic nerves yielded 0.5 c.c. and a further 60 minutes' stimulation gave 1.1 c.c. of secretion.

Cocaine augumented the secretory response of the stomach to rhythmic stimulation of the splanchnics. In a typical experiment (May 16, dog 8.1 kilos) stimulation for two hours before cocaine gave 1.8 and 1.8 c.c. of alkaline mucus. After intravenous administration of 15 mg. cocaine hydrochloride similar stimulation for two hours gave 3.0 and 3.0 c.c. The peptic power of the acidified mucus was very low. The rise of blood pressure during stimulation after cocaine was greater than before.

Effect of epinephrine. A solution of epinephrine (Parke, Davis & Co.), 1:5,000 or 1:10,000, was injected intravenously at regular intervals—0.5 c.c. every five minutes. The first injections of epinephrine usually somewhat inhibited the scanty spontaneous secretion of mucus, but subsequent injections definitely increased it. Thus in the Experiment of April 28, on a cat of 3.5 kilos, the mucoid secretion in two control hours was 0.2 c.c. and 0.25 c.c., but after the injection of epinephrine it rose to 0.7 c.c., 1.6 c.c. and 2.0 c.c. in the next three hours. The following control hour gave 0.2 c.c. only, and the two subsequent hours of stimulation with epinephrine gave 0.6 c.c. and 2.0 c.c. The total chlorine content of the secretion activated by epinephrine varied between 561 to 581 mg. per cent; the alkalinity ranged from 8.0 to 10.4 milliequivalents; and the peptic power rose somewhat, i.e. from 16 Mett's units in the control hour to 64 and 99 Mett's units after epinephrine injection, but was still very low.

Stimulation of partly degenerated splanchnic nerves. In order to separate the vasoconstrictor effect of stimulation from its secretory effect, as has been done by previous investigators (Volborth and Kudriawzeff, 1927), the splanchnic nerves were severed aseptically in dogs and cats below the diaphragm and above the coeliac ganglion by means of bilateral lumbar incision. The animals were experimented upon at varying intervals after operation, i.e. from 48 to 96 hours. It was noted that the vasoconstrictor fibres of the splanchnic nerves undergo degeneration more quickly in the cat than in the dog, although a certain amount of individual variation in this respect was noted in different animals.

The animals were prepared in the usual way for an acute experiment. The first observation was a spontaneous secretion of alkaline mucus, which occurred at a regular rate (e.g. 0.9 c.c. to 1.0 c.c. hourly for six hours in a cat of 3.6 kilos 48 hours after splanchnectomy, and somewhat less in other experiments). The peptic power of the secretion was low (16 to 35 Mett's units).

These data are not in agreement with those of Ishido (1922), according to whom the section of the sympathetic chain between the eighth and ninth dorsal segments did not produce any marked changes in the secretion from a Pavlov pouch in a dog. It must be remembered, however, that we were dealing with the secretion from the whole stomach, whereas Ishido collected it from the pouch only.

Electrical stimulation of partly degenerated splanchnic nerves gave in the majority of our experiments a very moderate but definite increase in the secretion (from 0.6 or 0.7 c.c. to about 1.0 c.c. per hour).

A typical experiment showing the effect of epinephrine is given in Table II. Intravenous injection of this drug at first caused a temporary inhibition of the secretion (4th hour of the experiment) which was probably due to vasoconstriction (Hess and Hundlach, 1920; Rothlin, 1920), the blood pressure rising to 210-215 mm. Hg. Further injection of epinephrine after half-an-hour's rest produced a definite increase in the secretion. Another remarkable feature was the marked rise in the digestive power of the mucus (from 16 to 320 and 256 Mett's units) and the change in its reaction from alkaline to faintly acid.

TABLE II

Secretory effect of suprarenine: stomach secretion.

Exp. April 21, 1932.

Cat, 4.1 k. Ether, chloralose and urethane. Splanchnic nerves sectioned 48 hours previously. Fed milk only on the day before. Oesophagus tied in neck; vagi sectioned in neck; pylorus ligated. Stomach reaction slightly acid.

Sample No.	*Time* min.	*Vol.* c.c.	*Peptic Power* Mett's units	*Reaction*	*B. P.* mm. Hg	*Remarks*
1	60	1.3	400	Neutral	110	Mucoid secretion.
2	60	0.8	35.2	Alkaline mucus	80	Control, no stimulation.
3	60	0.7	16	do.	82	
4	60	0.3		do.	80	0.5 c.c. 1:5,000 epinephrine every 5 min. B. P. 210.
5	60	0.5	16	do.	76	½ hr. rest, ½ hr. stimulation with epinephrine.
6	60	1.0	320	Very faintly acid mucus	68	do.
7	60	1.5	256	do.	72	do.
8	60	1.1	256	do.	60	do.
9	60	1.6	256	do.	58	do.

It was noted that cocaine sensitised the partly degenerated nerves to electrical stimulation, but had hardly any effect on the course of the spontaneous secretion of mucus.

Intravenous injection of ergotamine methansulphonate (Sandoz) greatly diminished the effect produced by stimulation of partly degenerated splanchnic nerves. Thus in one experiment (March 24) two control hours of splanchnic stimulation in a cat of 4.2 kilos gave 1.2 c.c. and 1.2 c.c. of neutral and slightly alkaline mucus. During the next two hours, when 8 mg. of ergotamine were introduced intravenously, the secretion fell to 0.2 c.c. and 0.35

c.c., and became slightly acid. During the succeeding control hour, 1.1 c.c. of acid mucus were secreted.

Stimulation of the splanchnic nerves when the stomach is divided into portions. In post-mortem examinations of the stomachs of dogs and cats after long-continued splanchnic stimulation, it was repeatedly observed that the greatest amount of mucus was adhering to the mucous membrane in the pylorus and antrum of the stomach. There was somewhat less in the body of the stomach, while the fundus showed the least amount, that mucus often being very thick and tenacious. The reaction of the different parts of the stomach varied correspondingly from alkaline in the pylorus to slightly acid in the fundus.

These observations led us to believe that the response to sympathetic stimulation varied in *quantity* and perhaps in *quality* in different parts of the stomach. To test this, experiments were performed in which the stomach was divided into three sections: (1) the pylorus (4 cm. from the pyloro-duodenal junction in the dog and 2.5 cm. in the cat), (2) the body, and (3) the fundus. Small metal fistulae were inserted into the posterior wall of the body and fundus pouches, and a glass cannula was tied into the pyloric part, a small incision being made in the duodenum.

From Table III it may be seen that stimulation of the splanchnic nerves as well as injection of epinephrine produced a greater secretion of mucus from the pyloric part than from the body of the stomach, while the secretion from the fundus was very much less than from the other parts. These results are more striking when the capacities of the respective pouches are taken into account. Two possible sources of the mucus secreted under the influence of the splanchnic nerves are: the surface epithelium and the special mucoid cells of the gastric glands, which Aschoff (1923) calls "*Zwischenzellen*", and of which there is an increasing number in the gastric glands towards the pyloric part of the stomach. Our results seemed to indicate that the mucus secreted under splanchnic stimulation is derived from the gastric glands and not from the surface epithelial cells. If the reverse were true, a greater amount of mucus would be secreted by the body and the fundus, which have a larger surface, than from the pyloric part. Moreover, the mucus is not pressed out by the movements of the stomach from the folds of the mucosa, where it might have accumulated previously. By means of a glass window sewn into the anterior surface of the stomach it was observed that during the stimulation of the splanchnics no movements of the mucosa nor of the stomach wall occurred. Nevertheless the formation of a thick layer of jelly-like mucus could be seen, which gradually filled the hollows between the folds.

TABLE III

Stomach divided into three sections.

	Fundus Pouch	Body Pouch	Pyloric Pouch
Exp. June 22 Cat	Capacity 10 c.c	Capacity 24 c.c.	Capacity 4.5 c.c.
Splanchnics stimulated for 7 hrs.	Total Secretion 1.0 c.c.	Total Secretion 3.6 c.c.	Total Secretion 7 c.c.
Exp. June 1 Dog	Capacity 26 c.c.	Capacity 45 c.c.	Capacity 5 c.c.
Epinephrine 1:5,000 for 7 hrs.	Total Secretion 0.25 c.c.	Total Secretion 3.6 c.c.	Total Secretion 4.4 c.c.

Vagus stimulation and secretion of mucus. It was demonstrated by Vineberg (1931) that different types of gastric secretion could be obtained in the dog by varying the strength of the induction current used to stimulate the vagi, *viz.*, a mucoid secretion with weak currents and regular gastric juice with strong currents. He suggested that the vagus possibly contains a variety of fibres, each innervating particular cytological elements of the gastric mucosa, and that these fibres may be activated by induction currents of different strengths. Heinbecker and O'Leary (1933) demonstrated, in the vagus nerve of the cat and turtle, three potential complexes, two of which might be associated with thinly myelinated and non-myelinated autonomic motor fibres.

Since Kiss (1931, 1932) challenged the established division of the autonomic nerves into sympathetic and parasympathetic, believing that all cranial autonomic nerves belong to the sympathetic nervous system, an inquiry into the nature of the mucus-secreting fibres of the vagus seemed desirable. First, Vineberg's findings concerning the two kinds of gastric secretion in the dog were confirmed in cats. To determine whether the hypothetical sympathetic fibres of the vagus might be responsible for the secretion of the gastric mucus, ergotamine and atropine were employed.

Intravenous injection of ergotamine methansulphonate (Sandoz) in doses of 5 to 8 mg. did not inhibit the secretion of mucus produced by weak rhythmic stimulation (coils 10.5 and 9.75 cm.) of the vagi in the neck. There was even a slight increase in the secretion, due probably to vasodilation. Thus in a cat of 3.2 kilos (Experiment of March 10), during two control periods of 60 minutes each, 1.0 c.c. and 2.4 c.c. of acid mucus were obtained. After the intravenous administration of 8 mg. of ergotamine methansulphonate, rhythmic stimulation of the vagi with a current of the same strength gave 3.2 c.c. and 3.5 c.c. respectively.

Under analogous circumstances, in a cat of 4.4 kilos (Experiment of March 2), intravenous administration of atropine sulphate (4 mg., 2 mg. and 3 mg. with half-an-hour between the injections) diminished the secretion of acid mucus by half, as may be seen from the following figures. The hourly secretions of mucus were: before atropine, 2.8 c.c. and 3.2 c.c.; after atropine, 1.5 c.c., 1.75 c.c. and 1.4 c.c. The partial inhibition of the secretion of mucus after the atropinisation of the animal might have been due to an incomplete paralysis of the motor vagus-fibres of the stomach. This is borne out by the fact that to the end of the experiment the reaction of the mucus was acid, i.e. much of the secretion collected after the injection of atropine might have been due to the slow expulsion of mucus already formed during the previous periods of stimulation.

Consequently, from these experiments with ergotamine and atropine it must be concluded that weak stimulation of the vagi in the cat or dog activates a mucus secretion through stimulation of certain fibres—not sympathetic fibres—contained in the vagus.

DISCUSSION

The results of this investigation would seem to show the mucus alkaline fluid produced by splanchnic stimulation to be a true secretion. The progressive diminution of the organic material in the secretion during prolonged stimulation and the maintenance of the concentration of the inorganic parts at the same level during the whole secretory period support this view, as does also the absence of movements in the gastric mucosa during splanchnic stimulation or administration of epinephrine.

Volborth and Kudriawzeff (1927), the only other investigators who employed rhythmic stimulation of the

splanchnic nerves in the dog, obtained from the stomach small amounts of an acid secretion. In their experiments, however, they did not give titration values of the acidity, nor state the characteristics of the secretion obtained. They did not stimulate the nerves for such long periods as are frequently necessary in order to obtain the typical results, and, in some of their experiments, excluded the pyloric part of the stomach.

The mucus obtained by weak stimulation of the vagi and by stimulation of the splanchnic nerves seems to be derived from different sources. In the former case, a fair secretion of mucus was obtained after exclusion of the pyloric part of the stomach (Vineberg, 1931), and the secretion coincided with the movements of the gastric mucosa. In the latter case, the body, and more especially the fundus of the stomach, produced much less secretion than the pylorus.

Although in this investigation no secretion of acid gastric juice was obtained during splanchnic stimulation, Volborth and Kudriawzeff (1927) have demonstrated that an acid gastric secretion can be produced through the action of the sympathetic nervous system. Inasmuch as we cannot confirm this without special experiment, it may be mentioned that in one of our experiments (Table II) intravenous administration of epinephrine in a splanchnectomized animal changed the reaction of the mucous secretion of the stomach from alkaline to faintly acid and increased the digestive power of the secretion.

The present investigation did not confirm Bickel's (1925) theory that the sympathetic nervous system has the major rôle in the production of enzymes by the gastric glands ("trophic" function), whereas the parasympathetic nervous system plays a secondary part influencing chiefly the secretion of water and hydrochloric acid ("secretory" function). It was repeatedly demonstrated that the mucoid, gastric secretion produced by splanchnic stimulation or by administration of epinephrine possessed an extremely *low peptic* power, whereas strong stimulation of the vagi produced gastric juice having an extremely *high digestive* power.

There is not sufficient evidence to interpret the "paralytic secretion" of gastric mucus after bilateral section of the splanchnic nerves as the result of the removal of the secretory-inhibitory influence exerted by the sympathetic nervous system on the gastric mucosa. It is more probable that this phenomenon depends on the altered vascularisation of the stomach after splanchnectomy.

SUMMARY

1. Long-continued, rhythmic stimulation of the freshly-sectioned splanchnic nerves with an induction current, in dogs and cats, produces a steady secretion of alkaline mucus possessing a low digestive power. The same effect is obtained whether the stimulation is produced by currents of high or of low frequency. Repeated injection of small doses of epinephrine has an effect similar to that of splanchnic stimulation.

2. Twenty-four to seventy-two hours after aseptic section of the splanchnic nerves below the diaphragm, there is a spontaneous secretion of alkaline mucus in the stomach.

3. Electrical stimulation of the partly-degenerated splanchnic nerves, as well as repeated injections of epinephrine, causes a definite increase in the volume of the "paralytic mucous secretion".

4. Atropine does not abolish the adrenalo-sympathetic mucous secretion; cocaine increases the response of the mucosa and ergotamine inhibits it.

5. Separation of the stomach into three parts—fundus, body and pylorus—indicates that the pylorus is the chief source of the sympathetic mucous secretion, the body of the stomach being less prolific in the secretion of mucus and the fundus very much less so.

6. Weak stimulation of the vagi produces a mucous secretion from the stomach of the dog and of the cat. Atropine inhibits this secretion, whereas ergotamine has no effect on it, indicating that the secretion is due to stimulation of parasympathetic fibres, and not of sympathetic fibres, present in the vagi.

The writer wishes to express his appreciation of the very helpful criticism and advice which he has received from Dr. B. P. Babkin during this work.

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RÔLE OF THE SYMPATHETIC NERVOUS SYSTEM IN GASTRIC SECRETION*

By

STEWART G. BAXTER
MONTREAL, CANADA

IT WAS previously demonstrated (Baxter, 1933) that rhythmic stimulation of the splanchnic nerves and also long-continued injection of epinephtine in small doses produced a slow secretion of alkaline mucus from the stomach in cats and in dogs. Section of the splanchnic nerves induced a "paralytic secretion" of gastric mucus.

In the present investigation, the influence of the sympathetic nervous system on the secretion activated through the parasympathetic nervous system and by some chemical substances has been studied.

In the literature reports concerning the effect of section of the splanchnic nerves on gastric secretion are contradictory. Pavlov and Schumow-Simanowski (1895) reported that section of the splanchnics in the dog had no effect on the quantity of the secretion obtained by sham-feeding, but that the content of total solids in the secretion did not rise so sharply as in the normal dog. Section of the anterior and posterior spinal roots between the 4th and 9th spinal segments (Schupfer, 1906), removal of the coeliac plexus (Gaultier, 1907), section of the splanchnic nerves (Gaultier, 1907; Foà, 1927; Moll and Flint, 1928; Trinchera and Rindone, 1930) resulted in an increase in the free and the total acidity of the gastric contents. According to Ishida (1922), however, section of the sympathetic chain between the 8th and 9th thoracic vertebrae had practically no effect on the secretory activity of a Pavlov pouch in a dog. Brown (1933) tested the acidity, without determining the volume, of the gastric secretion, after histamine administration, in cats in which the preganglionic sympathetic fibres had been sectioned or the coeliac ganglion removed (experiments with the alcohol test meal were not satisfactory). She did not observe any significant change in the free or total acidity of the gastric contents. Hess and Faltitschek (1924, 1925) found that injection of a 1 per cent solution of novocaine and epinephrine into the 7th and 8th dorsal segments increased the gastric secretion in normal persons but not in gastric ulcer patients. Pieri and Tanferna (1932) repeated this work with entirely different results. According to them, the paravertebral injection at the 7th and 8th dorsal segments, as also resection of the sympathetic rami of these segments, both in normal persons and gastric ulcer patients diminished the free and the total acidity and the peptic activity of the gastric secretion (Ewald test meal or histamine).

METHODS

In the present investigation, besides the acute form of experiment previously described (Baxter, 1933), experiments were carried out on two cats with oesophagotomy and a gastric fistula. These animals were found to be very satisfactory for chronic experiments of this nature. After the animals had completely recovered from the preliminary operation, a series of control experiments was performed on them. Both major splanchnic nerves then were cut aseptically by means of bilateral lumbar incisions.

RESULTS

"Paralytic" secretion and sham feeding. Seventy-two hours after splanchnectomy, when the animal was placed in the stand in a fasting condition, there was a small continuous flow of mucoid secretion, occurring at an even rate (0.6 to 0.9 c.c. per hour) for several hours. This secretion was thick and slightly opaque. There was no free acid, the total acidity ranged from 80 to 90 mg. per cent, the reducing power was high (95 per cent glucose), and the digestive power on acidification was unusually high, averaging from 576 to 784 Mett's units.

The "paralytic" secretion lasted for about two weeks, gradually diminishing. The acidity of the secretion slowly rose and on the tenth day after the operation reached 0.183 per cent (free) and 0.313 per cent (total), whereas there was a decrease in the digestive power (which ranged between 256 and 400 Mett's units) and also in the concentration of dissolved mucin (55.6 per cent glucose). Ten to fifteen days later, i.e. about one month after the operation, the paralytic secretion practically ceased.

Routine sham feeding with meat for 15 minutes during the first few days after the operation gave a smaller secretion than had been obtained before the operation. Later, the volume returned to normal. There were, however, some changes in the composition of the juice.

By way of example, we shall quote data obtained from one of the animals in which the observations were continued for two-and-a-half months after splanchnectomy. The free and the total acidity in this animal were somewhat lowered (free HCl, average before section of the splanchnics, 375 mg. per cent; after the operation, 335 mg. per cent—A decrease of 10.6 per cent; and total HCl, average before operation, 513 mg. per cent; after operation, 452 mg. per cent—a decrease of 11.9 per cent). There was no significant change in the concentration of Cl in the gastric juice after section of the splanchnic nerves, the average being 593 mg. per cent before operation and 581 mg. per cent after operation—a decrease of 2.0 per cent.

Only in the first experiment, four days after section of the splanchnic nerves, was a decrease in the total output of pepsin noted. Although the actual concentration of the enzymes was rather high (256 to 400 Mett's units), this result was undoubtedly associated with a decreased volume of secretion, and no particular stress can be laid on it. In the subsequent experiments, as may be seen in Fig. 1, the main difference was found to be in the distribution of the output of pepsin during the course of the secretion. Instead of a gradual rise to a maximum in the fourth ten-minute period as in the normal animal, the maximum output after section of the splanchnic nerves occurred in the first period; the output of pepsin declined gradually during the next two periods, and then fell sharply till the end of the experiment. On the whole, the digestive power of the juice did not diminish after splanchnectomy.

The average total output of dissolved mucin was higher in the post-operative experiments, but it declined more rapidly than in the pre-operative experiments, especially in the first 10 minutes of the secretion (in post-operative cases from 150 mg. per cent to 75 mg. per cent; in pre-operative cases from 80 mg. per cent to 40 mg. per cent).

Effect of epinephrine and splanchnic stimulation on histamine gastric secretion. Some acute experiments were performed on anaesthetized cats. Different results were obtained if epinephrine (0.5 c.c. 1:5,000 to 1:10,000 every 5 minutes during periods of from 45 to 90 minutes) was injected intravenously during profuse gastric secretion from histamine (1 mg. to 3 mg. subcutaneously), the

*From the Department of Physiology, McGill University, Montreal, Canada.

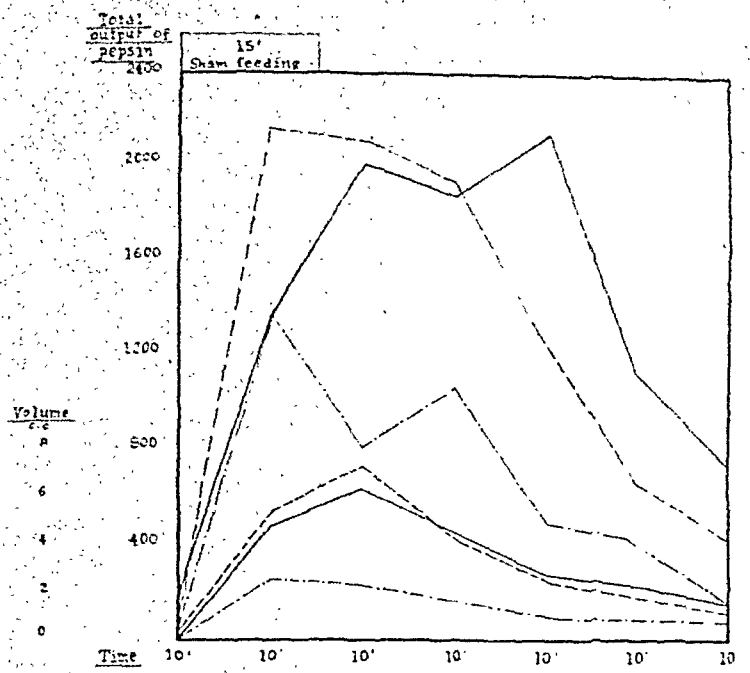


Fig. 1—Total output of pepsin (upper curves) and volume (lower curves) in 10-minute periods.

Key:

———————————Average before operation.

— — — — — — — — —First experiment after section of splanchnic nerves.

— — — — — — — — —Average in all subsequent experiments.

secretion averaging 10.5 c.c. in half-an-hour, or during slow secretion, measuring from 2.5 c.c. to 3.0 c.c. in half-an-hour. In the first case, epinephrine had apparently no marked effect either on the course of the histamine secretion or the composition of the gastric juice. This is easily understood because the secretion activated by epinephrine is itself rather scant. In the second case, there was a slight increase in the volume of the secretion, a slight decrease in the free acidity, no change in the total acidity, and a very moderate increase in the digestive power of the juice. The values for the digestive power (16-48-64 Mett's units) were such as are usually obtained with epinephrine or splanchnic stimulation.

A similar effect was produced on histamine gastric secretion by rhythmic stimulation of freshly-cut splanchnic nerves in anaesthetised animals. This increased particularly the content of dissolved mucin in the juice.

The effect of epinephrine (0.5 c.c. to 1.0 c.c., 1:10,000) on gastric secretion after histamine (0.5 mg. subcutaneously) was again tested on cats with oesophagotomy and a gastric fistula. The results were comparable on the whole to those obtained in the acute experiments. The free acidity fell somewhat (a decrease of 10 to 15 per cent) after the injection of epinephrine, the total acidity remaining unchanged. There was a slight increase in the reducing power and in the peptic power.

Histamine and sham feeding. Histamine (0.5 mg. subcutaneously), followed by sham feeding, gave in the cat a typical picture resulting from the combination of these two stimuli. Histamine, given subcutaneously, produced a copious secretion of highly acid juice with a low ferment and reducing power. Towards the end of this secretion, the animal was sham-fed for fifteen minutes. As a result, the free and the total acidity in some cases fell slightly and then rose to their former levels. The ferment and the reducing power rose sharply and maintained higher levels. After section of the splanchnic nerves the experiment was repeated and gave exactly the same results (see Table I).

Pilocarpine and sham feeding. Pilocarpine (0.5 mg. to 1.0 mg.), injected subcutaneously in a cat with oesophagotomy and a gastric fistula, produced somewhat different results from those obtained in dogs. In dogs, pilocarpine activated a flow of thick mucoid secretion with a very high enzyme content (Vineberg and Babkin, 1931). In the cat, the secretion was also scant (1.8 c.c. to 3.4 c.c. in 30 minutes) and mucoid, but the ferment power often fell progressively during the experiments and reached low levels (e.g. 16 Mett's units). The reducing power of the secretion tended to decline, also the free and the total acidity, while the total Cl content was lower than that of the juice from histamine or sham feeding (488 mg. per cent in one experiment, 569 mg. per cent in another—cf. with data in Table I). When sham feeding was begun, after the pilocarpine secretion declined, all the values rose to a higher level and remained there. After section of the splanchnic nerves there were no notable changes in the response to pilocarpine and sham feeding. In connection with these facts, it is interesting to note that Bolton and Goodhart (1931) obtained a secretion of gastric mucus in anaesthetized cats after atropinization. It seems that, in the cat, pilocarpine does not act on the vagus endings, as is usually claimed.

TABLE I.

Histamine and sham-feeding juice after splanchnectomy.

Exp. May 12, 1932.

Cat. No. 2. Splanchnic nerves sectioned May 6, 1932. Histamine and sham feeding.

Sample No.	Time min.	Vol. c.c.	Free HCl mg. %	Total HCl mg. %	Total Cl mg. %	Reducing Power % glucose	Peptic Power Mett's units	Remarks
1	30	0.4					400.0	Control.
2	15	1.7				35.6	256.0	½ mg. histamine subcutaneously.
3	15	4.0	355	465	590	12.8	8.0	
4	10	4.1	397	511	598	6.4	2.5	
5	15	4.0	415	512	601	4.0	0.8	
6	15	3.0	421	514	604	6.4	0.0	
7	15	1.3						
8	10	4.2	427	531	627	27.8	310.0	Sham feeding 15 min.
9	10	5.1	416	540	627	19.2	256.0	
10	10	5.1	446	565	635	35.2	210.0	

CONCLUSION AND SUMMARY

This investigation establishes the fact that the sympathetic nervous system does not play an essential part in the first, or nervous, phase of gastric secretion. It would seem that this phase is mediated chiefly through the parasympathetic nervous system, a fact long known. However, in the present investigation, as mentioned above, some changes were noted in the composition of the sham-feeding juice after splanchnectomy. These may have been due to the continuous "paralytic" secretion of mucoid fluid resulting from section of the splanchnic nerves.

It seems that the sympathetic nervous system has some relation to the secretion of gastric mucus. It may be, however, that this function of the sympathetic nervous system is manifested to a certain extent in the first phase of gastric secretion. Thus Savitch (1922) demonstrated on a dog with a Pavlov pouch that feeding with "Zwieback", during the course of the secretion on milk, raised the volume of the secretion and markedly lowered the free and the total acidity of the juice. He attributed this to the greater amount of mucus present in the juice, this secretion being activated reflexly from the mouth cavity.

Another important conclusion which may be drawn from these experiments is that the "trophic" effect on the peptic glands is exerted by the vagus and not by the sympathetic nerves. This is in agreement with the view that

the *parasympathetic* and *not the sympathetic* nervous system conveys "trophic" impulses to the gastric and salivary glands (Babkin, 1931 a and b), but is contrary to the opinion of Bickel (1925), who claimed that the sympathetic system plays the major rôle in the control of the secretion of organic material and enzymes by the gastric glands. If Bickel's supposition were correct, then, for example, sham feeding after histamine (see Table I) should not produce as great an increase in the peptic power of the gastric secretion *after* section of the splanchnic nerves as it did when these nerves were *intact*.

The writer gratefully acknowledges the helpful advice and criticism which he has received from Dr. B. P. Babkin during this work.

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Section III.

Nutrition

Contributions by

CLIFFORD J. BARBORKA

NUTRITION IN HEALTH AND DISEASE*

By

CLIFFORD J. BARBORKA, B.S., M.S., Sc.D., M.D.

CHICAGO, ILL.

NUTRITION has definitely established itself as a science in the past thirty years. More precise knowledge has accumulated regarding the requirements of food to maintain the proper nourishment of the body than in the previous century.

When one delves into the study of man, he emerges with the feeling that there have been very definite epochs in the evolution of our diet. Races of people have changed very definitely and radically their habits of eating by some unforeseen circumstance. Custom determines the arrangement of the meals and kind of foods eaten, but the experience of the race governs the custom. In reflecting upon the food habits of our ancestors one may feel that they derived adequate nourishment without knowing the ash content of the orange, the caloric value of bacon and eggs or the vitamin property of tomatoes. This, perhaps, is true but great changes have taken place in the past thirty years in the production and selection of food. The assumption is expressed, often, that the normal person, when free to choose, will by instinct select the foods best suited to his needs. Within certain limits this may be true, but, generally speaking, the question is not so much what he will select as it is that economic force and necessity make him get what he can for sufficient nourishment.

There is a great diversity of diets upon which people, in various parts of the world, subsist and upon which they manage to do fairly well. For the past decade the American diet has had a growing tendency to consist chiefly of meat, eggs, fine, white patent-flour, potato, sugar and fats, and products from seeds like peas, beans, rice, oats and corn. One of the greatest changes in the dietary habits of the people of the United States is the annual per capita consumption of sugar. In 1823 the consumption of sugar was 8.8 pounds per capita; in 1931, 108 pounds per capita. This means that over one-fifth of our daily energy requirements is made up of a vitamin-free food. The production and selection of a large part of the remainder of the foods have been greatly influenced by food industries. A large percentage of foods thus prepared have lost much of their vitamin potencies in the refining process to which many modern foods are subjected. As the consumption of carbohydrate has increased, the use of protein, especially that from meat, has decreased. Thus, the American diet contains a large proportion of concentrated food, low in vitamin, residue and alkaline minerals, and high in carbohydrate and acid minerals. There has been a tendency to an inadequate amount of the bulky residue-containing foods, such as fruits and vegetables. As a result of propaganda as to fruits and vegetables, the pendulum probably is now swinging in the opposite direction.

The term "protective foods" has been applied to milk and leafy vegetables, since they correct the calcium and vitamin deficiencies of the common American diet. The greater use of "protective foods" is becoming more widespread every day and milk, fresh meats, eggs, fruits and vegetables are available in the smallest places throughout the year.

A large majority of adult patients who consult the average physician are interested in diets. Food is being recognized as a most important social factor in the life of every human being. Events are occurring today that indicate how international relationships are affected by our universal dependence upon the adequate supply and distribution of food. Medical treatment is resolving itself more and more into modifications of food ingested. As a matter of fact, the abundance or dearth of food, its cost and distribution affect indirectly but intimately the therapy of every patient.

DIET IN HEALTH

In order to formulate proper diets in the treatment of disease, it is first necessary to have a comprehensive grasp of the nutritive principles of diet in health. All the newer knowledge of the nutritive needs of the human body are the result of experimental studies on animals, correlated with the application of these studies on human subjects.

There are certain essential requirements that all diets must possess in order adequately to protect and maintain health. These requirements are:

1. Adequate protein
2. Mineral elements
3. Vitamins
4. Sufficient calories for energy requirement
5. Water

ADEQUATE PROTEIN

The ingestion of food usually is considered to satisfy two physiologic requirements: First, to furnish raw material for the growth and repair of body tissues, and second, to furnish energy for the processes of life. For the first purpose, protein alone will suffice. One of the most confusing problems of nutrition both in health and disease is the question as to what is the adequate protein of the diet. Many factors affect the level of protein metabolism and although opinion varies, we consider 1 gram for each kilogram of body weight adequate for the average normal adult.

MINERAL ELEMENTS

The hidden mysteries of cell-life which are slowly being unraveled are intimately connected with inorganic mineral elements. The body contains about twenty of these elements in appreciable quantities. Adequate amounts are essential. The American dietary is probably more deficient in calcium than in other ingredients. The requirement approximates 0.75 to 1 gm. which is the amount contained in 1 liter of milk (1 quart). The daily food of an adult should contain about 15 mg. of iron. Iron is present in lima beans, peas, unmilled wheat, lean beefsteak, spinach, oatmeal, raisins, eggs, and green vegetables. The ordinary diet is not deficient in iron. The importance of copper has been realized from the work of investigators at the University of Wisconsin who feel that deficiency of this element interferes with the assimilation of iron.

The amount of phosphorus required by adults has been estimated to approximate 1 to 1.5 gm. a day. It is essential to the nuclear constituents of blood and lymph plasma. The dietary is often deficient in phosphorus despite its wide distribution as an inorganic element in foods.

In certain areas of endemic colloid goiter, the water and vegetables raised from the soil are deficient in iodine. The normal thyroid gland stores about 25 mg. of iodine. Marine believes that the yearly requirements probably do not exceed 50 mg. In iodine deficiency this mineral, in the form of iodized salt, may be administered. Plummer gives a few drops of compound solution of iodine once a week and feels this is adequate. Magnesium, sodium, and potas-

*Department of Medicine, Northwestern University Medical School, Chicago, Illinois.

sium are usually not lacking in ordinary diets. In fact, the chief element to take thought of in the selection of foodstuffs is calcium.

VITAMINS

Recent investigations, the first full report in 1912, have developed the fact that food of sufficient nutrients, minerals and water is not necessarily adequate to meet all the requirements of nutrition. Thus it appears that certain substances called "vitamins" that are present in the normal dietary in infinitesimal quantities, far too small to yield any contribution to the energy supply of the body or to the bulk as structural elements of the tissues, have great importance in the body's nutritional functions. It is not surprising that popular experience of nutritional agencies which function in such minute quantities and are consumed unconsciously in every adequate diet.

In recent years, much advancement has been made in the knowledge of vitamins, both as to their chemical characteristics and their biological action. Even though a greater part of this knowledge is the result of animal experimentation, it is now possible to make practical application of them in human nutrition. For many years, it has been known that prolonged deficiency of certain vitamins from the dietary hinders the growth of young animals and may be the cause of various diseases in adults. Also, certain human diseases are known to be due to the absence of one or other of the vitamins.

The principal functions of vitamins in human nutrition are:

1. To promote and maintain health and optimal growth.
2. To prevent or cure deficiency disease.

A deficient intake of one or more of the vitamins does not always result in a specific disease, but it may bring about changes of specific structure which make for inevitable susceptibility to a latent deficiency disease.

Although Vitamin A may not hold the direct controlling relation to any one disease that Vitamin B holds to beriberi and Vitamin C to scurvy, yet it is probable that of the three, Vitamin A is a factor of greatest practical significance in nutrition and health, because so many of our staple foods are poor in Vitamin A, and because the dietary low in this vitamin causes a poor condition in nutrition and increases susceptibility to many infectious diseases.

It has been found repeatedly by many investigators and in many different species, including man, that a diet poor in the fat-soluble Vitamin A leads to weakness in many respects. Not only the eyes, but the appetite, the digestion, the air passages, the lungs, the bladder, the skin, the sinuses, and the ears are likely to suffer when the food is poor in respect to fat-soluble Vitamin A.

Since the animal can store Vitamin A in relatively greater proportion than Vitamin B or C, and since the effects of a shortage of Vitamin A are less specific and more widespread, the results of experiments with Vitamin A have, in many cases, given confusing results, and failed to correct interpretations. Because of these facts the great importance of this vitamin has not been fully appreciated. We now have good reason to believe that a surplus of Vitamin A in the body is not simply a reserve to be used at some future time, but that it actually increases the vigor and the ability of the body to resist disease.

Apparently neither the liver nor the body as a whole ever store enough Vitamin B to meet the requirements of nutrition for any considerable length of time without receiving new supplies of it in the food.

Not only is the chemical nature of Vitamin B still unknown, but just what should be included under the term has become largely a matter of individual preference. Almost before the novelty of the dual nature of the B-complex had subsided, studies of highly purified fractions indicated the possibility of several other components in the complex, although eventually they may be shown to be identical.

Within the last two years, rapid advance has been made in the knowledge of the chemical nature of Vitamin C. Crystalline material has been obtained from concentrated lemon juice and orange juice, which exerts a powerful antiscorbutic action on experimental animals. The fresh cortex of the suprarenal gland has been shown, also, to be a most potent source of anti-scorbutic factor. Karrer and associates claim that the crystalline preparations are an organic acid called "ascorbic acid", although there is some hesitation in identifying it with Vitamin C. It appears that from the chemical studies of Vitamin C an explanation of the mechanism of protection against scurvy may be forthcoming. We have gained a much clearer understanding of the anti-scorbutic foods, particularly the relation of various processes and method of preparation to which they are subjected.

A great deal of interest has been stimulated regarding the possible function of Vitamin D in regulating the absorption and metabolism of the bone-forming elements, calcium and phosphorus.

The discovery of Vitamin E is of practical importance to those engaged in the breeding of rats for experimental purposes. A number of workers are at present doing clinical investigation on human fertility. The only reports are those of Vogt-Moller, who have treated two women who had experienced four and five previous miscarriages with wheat germ oil. In both cases a successful pregnancy occurred.

It has been shown that Vitamins A, B, C, D, E and G are valuable for normal growth and health at all ages. They are particularly valuable to children. Their importance in the field of nutrition begins with pregnancy and lactation.

The *clinical features of deficiencies or absences of vitamins*, some of their excellent sources, and artificial concentrates known thus far are presented for review in the vitamin charts (Table I).

SUFFICIENT CALORIES FOR ENERGY REQUIREMENTS

Sufficient calories for energy requirements of the body are supplied by food which contains: (1) Carbohydrates, mostly vegetable in origin, sugars, starches, grains, cereals, and fruits; (2) protein, mostly animal in origin, meat, fish, eggs, milk and cheese, and (3) fat, partly vegetable, as olive oil and cotton-seed oil, and animal, as butter and lard.

Full appreciation of the importance of calorie values of foodstuffs dates back to Rubner. Actual determinations in the calorimeter have considerable variations, but for clinical purposes, considering material actually absorbed and utilized, we can use the calorie value of four calories for each gram of carbohydrate and protein, and nine calories for each gram of fat. Sufficient calories for the normal healthy adult are dependent on the manner in which each patient reacts to a given diet. With the development of the modern machine-age which has relieved hard physical exertion, the demand for a large caloric intake is lessened and greater is the need to emphasize the use of fruits and vegetables to make up adequate bulk.

WATER

The water in the body is derived from three sources: (1) by the fluids taken (water, beverages, milk, tea, coffee or soup); (2) by the water contained in solid foods, and (3) by the water produced in the body as a result of the oxidative processes of metabolism.

The functions of water are primarily based upon its usefulness as a solvent. It aids the digestive fluids in the absorption of food. It is a valuable adjunct in transporting

TABLE I

Vitamin	*Clinical Features of Deficiencies or Absences*	*Found in*	*Artificial Concentrates*
A Anti-infective Fat Soluble	Retardation of growth and development Diminished resistance to infection Failure of appetite and digestion Possible sterility due to failure of ovulation	Milk, cream, butter, eggs, liver, fruits, green vegetables, as cabbage, lettuce, peas, carrots, spinach and tomatoes	Halibut liver oil Cod liver oil Carotene
B_1 (or F) Anti-neuritic Water Soluble (less heat labile)	Impairment or loss of appetite Disturbed digestive processes Impairment of growth in lactation period May produce amenorrhea Beriberi or polyneuritis (nerve disease)	Fresh fruit juices, egg yolks, most vegetables, especially beans, peas, spinach and tomatoes; milk; whole grains or cereals	Brewer's yeast Wheat germ Rice polishings
B_2 (or G) Anti-pellagric Water Soluble (more heat labile)	Pellagra and pellagra-like conditions	Glandular organs, liver, kidney, spleen, lean meats; vegetables as beet green, potato, spinach, turnip, greens; eggs, milk	Brewer's yeast
C Anti-scorbutic Water Soluble (heat sensitive)	Scurvy Decalcification of bones Decay of teeth Loosening and shedding of teeth	Citrous fruits, as orange, lemon, and lime; raw vegetables as tomatoes, lettuce, peas, cabbage and spinach	Orange juice Lemon juice Fresh cortex of suprarenals
D Anti-rachitic Fat Soluble	Rickets (bone disease) Faulty absorption of calcium and phosphorus in the body Defects in teeth (caries, poorly calcified teeth) General muscular weakness and instability of nervous system	Milk and egg yolks	Ultra-violet light Cod liver oil Tunafish liver oil Irradiated ergosterol Halibut liver oil
E Anti-sterility Fat Soluble (heat stabile)	Failure in reproduction	Fresh meat; green vegetables; whole wheat; milk fat	Wheat germ oil

soluble substances in the blood and lymph. It aids in the excretion of soluble waste products of the body. Water keeps the materials in the tissues in solution so that chemical reactions can take place and also maintains the proper dilution of salts in the tissues. The body temperature is regulated by water. Removal of excess heat is accomplished by evaportaion of water from the body surface.

Water is excreted from the body by the kidneys in urine, by the lungs as water vapor in the expired air and by the skin as sensible and insensible perspiration.

We suggest that from six to eight glasses of water be taken daily. This amount is variable, depending upon the fluids ingested from other sources, as well as the activity of the individual and the temperature of the environment. There is no objection to drinking water with meals provided it is not used to mechanically wash down the food. Large quantities of ice water inhibit digestion and are to be avoided.

THE ESSENTIAL REQUIREMENTS FOR ALL DIETS

The essential requirements all diets must possess in order to be adequate and protective to maintain health have been briefly discussed. In Table II are presented foods including the protective foods that serve as a basis to meet these essential requirements.

TABLE II

Foods that serve as a basis to meet essential requirements

1. Milk 1 pint
2. Egg One
3. Vegetables 3 large servings besides potato (one a green leafy vegetable)
4. Fruit 2 servings
5. Meat, fish, fowl 1 serving (2 ounces)
6. Butter 1½ squares (15 grams)

These foods should serve as a basis of all diets, and, if used in the amounts suggested, will be protective and will meet all the minimum requirements, except calories. The analysis of their contents is in Table III. They will average approximately 80 grams of carbohydrate, 45 grams of protein, 45 grams of fat and 900 calories.

Any additional foods may be chosen to make up the caloric needs depending upon the individual problem, and one will be assured that the diet will be adequate and all the essential requirements will be met.

TABLE III

Analysis of foods that serve as a basis to meet essential requirements

	Amount Grams	Carbohydrate Grams	Protein Grams	Fat Grams	Approximate content of Minerals—Grams		
					Calcium	Phosphorus	Iron
Milk	450	22	14	18	.540	.419	.0011
Egg (one)	50		6	6	.031	.090	.0015
Meat (lean)	60		15	9	.009	.162	.0023
Butter	15			13	.002	.003	
Vegetables, 3%	200	6	2		.114	.082	.0020
Vegetables, 6%	100	6	1		.047	.045	.0005
Fruit, 10%	100	10	1		.028	.022	.0004
Fruit, 15%	100	15	1		.021	.027	.0005
Potato	100	20	2		.014	.058	.0013
TOTALS		79	42	46	.809	.908	.0096

Calories 898

An example of a typical diet for one day, incorporating the foods that serve as a basis to meet the essential requirements with additional foods added to make up the caloric needs of the average normal adult weighing 150 pounds, is outlined. Whenever the demand for additional energy is required, the calories to cover this need may be supplied by simply increasing the amount of fats or carbohydrates or both.

A Typical Diet for an Average Normal Adult Weighing 150 Pounds

70 Grams Protein
2400 Calories

BREAKFAST

Fruit	1 serving
Cereal (cooked)	⅔ cup
Bacon	2 slices
Egg	1 egg
Butter	2 squares
Cream, 20%	¼ cup
Sugar	1 tablespoon
Beverage	

LUNCHEON

Egg (or egg substitute)	1
Potato or substitute	1 serving
Vegetable	1 serving
Salad:	
Fresh vegetable	1 serving
Salad Dressing with oil	1 tablespoon
Bread	1 slice
Butter	2 squares
Milk	1 glass
Fruit	1 serving

DINNER

Meat	1 serving
Potato	1 serving
Vegetable	1 serving
Fruit salad	1 serving
Bread	1 slice
Butter	2 squares
Milk	1 glass
Dessert	1 serving

DIET IN DISEASE

It is only within the last thirty years that diets accurately have been controlled and the quantities of carbohydrate, protein, and fat recorded. Even more interesting, is the fact that only within the last fourteen years has attention been called to the fatty acid-glucose proportions of the three foodstuffs, carbohydrate, protein, and fat. In consequence, it readily can be seen that only today can we begin to consider how best to distribute any given intake.

The greatest fault of dietetics today is the attempt to use a stock or printed list for a particular disease applied to all patients afflicted with the disease, irrespective of the particular needs of the individual patient.

As a simple understanding of the contents of an adequate and protective diet is the foundation essential for health, so individual dietetic education and instruction in measured diets has become the most important first step in the treatment of an increasing number of disorders in disease. Treatment by diet today must be considered from three angles: (1) *Qualitative diets;* (2) *estimated quantitative diets,* and (3) *weighed quantitative diets.* In the teaching of these methods, an ever-growing part is being played by the well-trained dietitian.

Simple qualitative diet means just the omission of certain articles of food, such as rough restriction of sugars and starches in a mild case of diabetes; or coffee, tea, and cocoa when a patient is nervous. For moderate reduction of weight in simple obesity, the gross fats and carbohydrates such as butter, cream, gravies, oil dressing, pastries, table sugar, breads, and perhaps, even potatoes and rice, should be curtailed. Many patients will be fortunate enough to derive sufficient relief from such simple omission and find it unnecessary to go into further details of management.

The distinction between *simple qualitative* and *quantitative diets* is not always made clear to the patient. Such distinction definitely must be understood in all cases in which patients fail to be improved by qualitative restrictions within a reasonable length of time, or to those cases in which diet is of paramount importance in relation to the disease.

A *quantitative diet* is one in which any article of food eaten should be thought of in terms of calories, carbohydrate, protein and fat, and in which the quantitative estimation of these values is imperative. No food should be eaten in unlimited quantities. Any article of food may be eaten provided it contains proportions of carbohydrate, protein or fat in amounts that can be incorporated in the total quantity of carbohydrate, protein, and fat that is allowed each twenty-four hours and does not displace any of the foods required to make the diet adequate and protective.

A quantitative diet may be etsimated in simple household terms such as tablespoonfuls, one heaping tablespoonful or two level tablespoonfuls being equal to one ounce. If this method of quantitative restriction is inadequate, then one must resort to the use of a weighed quantitative diet. This necessitates the use of food scales and an accurate knowledge of the carbohydrate, protein and fat composition of food. Many patients may feel this is a difficult task and resent the added work. It is well to caution patients needing quantitative weighed diets that successful dietary treatment cannot be achieved by a month's enthusiastic effort followed by a return to the old habits. Success depends on their acquiring a thorough knowledge of the fundamentals of dietetics and, under the physician's guidance and coöperation in developing and maintaining the new habits of food intake suitable to their individual needs. When these patients are convinced that a fair trial of weighing food is justified, they are soon astounded to find that weighing food is not so much of a task as they had anticipated. After several weeks, they are able practically to estimate their food proportions by the eye. They learn that the different foods have marked differences in weight and proportion to carbohydrate, protein, and fat. Finally, they learn that it is not difficult to juggle figures and make substitutions in the diet to increase its palatability and still keep the diet adequate and protective.

With the foregoing methods of application of dietotherapy, we present in Table IV an outline of diseases in which diet is of paramount importance in treatment and Table V the conditions in which diet is of varying importance.

TABLE IV

Diseases in Which Diet Is of Paramount Importance

Metabolic Disease:
- Diabetes mellitus
- Gout
- Overweight—obesity
- Underweight—malnutrition
- Nephritis

Diseases of Blood:
- Pernicious anemia

Diseases of Digestive Tract:
- Peptic ulcer
- Constipation

Deficiency Diseases:
- Food deficiency and chronic disease
- Nutritional edema
- Tetany—osteomalacia
- Pellagra, lack of vitamin B
- Beriberi, lack of vitamin B
- Scurvy, lack of vitamin C
- Rickets, lack of vitamin D
- Simple goiter, iodine deficiency

TABLE V

Conditions in Which Diet Is of Varying Importance

Diseases of Heart and Arteries:
- Heart
- Hypertension

Febrile Diseases:
- Typhoid
- Tuberculosis
- Pneumonia
- Other infectious diseases

Diseases of Esophagus and Stomach:
- Gastritis
- Gastric neurosis
- Hyperchlorhydria
- Achlorhydria and achylia
- Obstructive lesions of esophagus
- Obstructive lesions of stomach

Diseases of Liver and the Gallbladder:
- Cirrbosis (with ascites)
- Jaundice
- Gallbladder disease

Diseases of the Intestine:
- Diarrhea
- Flatulence
- Fermentation
- Putrefaction
- Mucous colitis
- Ulcerative colitis
- Diverticulosis and diverticulitis
- Sprue

Diseases of Blood:
- Secondary anemia

Diseases of Urinary Tract:
- Infections of urinary tract
- Calculi of urinary tract
- Oxaluria
- Phosphaturia
- Uraturia

Skin Disease
Epilepsy
Migraine
Arthritis
Pregnancy and Lactation
Dental Caries

It is impossible in so short an article to go into details of dietotherapy, but we wish briefly to point out the basic therapeutic factors at present considered essential in relation to a few diseases.

The *metabolic diseases* in which diet is of paramount importance are diabetes mellitus, gout, overweight, obesity, underweight-malnutrition and nephritis.

Probably no disease deserves greater credit for stimulating sound interest and developing dietetics than does *diabetes mellitus*. Prior to the discovery of insulin, diet was the only form of treatment and its discovery only served to increase the importance of diet. The actual method of procedure for the regulation of diet in the diabetic patient is dependent on the severity of the diabetes and whether or not there is associated acidosis. The diet varies from a simple *qualitative restriction* of carbohydrates to *quantitative weighed* diet with or without insulin. Varied proportions of carbohydrate and fat are used by different clinicians, some using high fat and low carbohydrate, others using high carbohydrate and moderately low fat with, of course, high doses of insulin. Most students of diabetes are fairly well agreed on the principle of protein restriction and use about 1 gm. of protein for each kilogram of body weight.

Dietary treatment in *gout* demands moderation in eating and drinking, and a low purine intake. In many instances, associated obesity demands reduction. Foods to be avoided are the meats, especially cellular meats such as sweetbreads, liver and kidney, broths and meat soups, as well as rich gravies and sauces, peas and beans, whole grain cereals including oatmeal; also coffee, tea and cocoa. The chief sources of protein to be used in this condition are milk, eggs and cheese.

Simple weight reduction of a few pounds usually can be accomplished by a qualitative restriction of gross fats and concentrated carbohydrates as previously mentioned. When more exact weighed dietary restriction is deemed necessary, regardless of the type of obesity, the following procedure may be carried out. First, the desired weight in the steps of reduction is set as an objective. This expected weight may be 20 to 40 pounds under the present weight. One gram of protein per kilogram of the expected weight is allowed. Eighty-five hundredths of a gram of carbohydrate per kilogram of the expected weight is allowed. The fat is then regulated in an amount to give the desired number of calories in the reduction program. Six hundred and fifty to 1,000 calories may be used. When the caloric intake is of the lower limits, it is necessary to give brewer's yeast, halibut liver oil and dicalcium phosphate to insure adequate protection of vitamins and minerals.

On such a program, by insuring a normal metabolizing mixture, and maintaining the *regime* an adequate period of time regardless of the calories given by mouth, the patients do not experience discomfort and will reduce their weight. Whenever it is possible, we prefer giving 800 to 1,000 calories in order to teach the patient better food habits.

Underweight is a term including varying degrees, from the underweight individual who is in perfect health to those who are actually emaciated as the result of starvation or disease. For simple cases of underweight, one often can gain weight by adding some of the typical concentrated foods that are high in energy value. Some cases may require careful diet supervision, emphasizing high caloric intake, high carbohydrate, moderate amounts of protein, moderately high fats easily digested with the adaptation of the bulk to allow concentrated foods.

There is a radical difference of opinion in the present day conception of the proper *diet for nephritis*. In the past, the thought primarily was focused upon the kidney and the possible damage of protein and products of catabolism. As a result, the patient was told to eat no meat. Recently, the trend of thought has been toward the patient himself and the upbuilding effects of protein with greater allowance of protein.

Except during emergencies, such as chronic cases with nitrogen retention or acute nephritis, the protein should not be lower than 1 gm. for each kilogram of normal weight. There is no great difference between the types of protein in red meats and poultry or other flesh protein. Because of the desire to reduce protein metabolism as low as possible, it is well to have a high intake of carbohydrate and less of fat because the protein-sparing properties of carbohydrate are greater than are those of fat.

In *acute nephritis* for the first few days it is well to restrict protein to 20 to 25 gm. per day and the total calories to a minimum. Volhard has had very good results with a so-called "hunger" treatment. Later, one can increase the protein to 40 gm. or more. Sufficient fluids must be given to afford proper drainage, but fluids should not be forced. The Karrell milk diet often is used during acute stages, adding fruit juices with sugar if more calories are needed. Later, more starchy foods are added, but the protein is limited for a long period, although not too prolonged, especially if plasm proteins are low. Of course, rigorous restriction of salt is necessary in acute cases.

In *chronic nephritis*, with edema, Keith advocated a diet which is very low in fluids and mineral content. The fluid intake is restricted to 700 to 1,000 c.c. daily and the salt intake from 0.5 to 2 gm. daily. There is no absolute experimental proof that a diet low in salt is indicated in nephritis that is *not* accompanied by edema. The average case is started on a 40 gm. protein diet. The presence or absence of nitrogen retention or of low serum protein determines the question as to the amount of protein increase that may be allowed.

The important, practical contribution of the studies of *nephrosis* is influence in the protein loss and the emphasis of the need of giving a liberal amount of protein, as much as 150 grams per day, to replace the loss of albumin in cases of edema when the phthalein output is good and there is no increase in blood urea or other evidence of renal incompetency.

The use of liver, or of the extract derived from it, in the treatment of *pernicious anemia*, introduced by Minot and Murphy in 1926, has revolutionized the outlook for

the disease. Koessler and his associates have used the high-vitamin diet. Since this work, Sturges, Isaacs, and Sharp have used desiccated gastric tissue, and Conner has used both raw and desiccated gastric tissue, apparently with the same results. It is probably best to give about 200 gm. of liver a day in the average case and up to 500 gm. a day in severe cases. Calf liver is preferable to beef liver because it is more tender and less sinewy, but any mammalian or fowl liver may also be used for variety. Since this work was begun, innumerable recipes for preparing liver have been devised in an effort to increase its palatability.

The dietary treatment for both *duodenal* and *gastric ulcer* is essentially the same. Probably in no disease has standardization in the diet had more of a vogue than in ulcer. All physicians are familiar with the Sippy regimen or its modifications.

"Deficiency disease" is a term that has been applied primarily to the results obtained from feeding experiments on animals produced by the lack of one or more vitamins. Similar conditions, such as *pellagra, beriberi, scurvy,* and *rickets* have been observed in man with vitamin deficiency. Table I points out the vitamins which prevent these conditions. Outside of pellagra, these conditions are rare and infrequently seen in the United States. The term "deficiency disease", however, should include in its scope not alone vitamin deficiencies, but those conditions in which one or more of the other nutrients—carbohydrate, protein, fats and minerals—may be lacking. Defects in diet may be only slight, but when followed for a long period of time may be responsible for various degrees of illness without an associated syndrome of any definite malady. The influence of food deficiencies on chronic disease is just beginning to be appreciated. Results can be observed either due to accidental or slight omissions of the adequate or protective foods, or one may see mild complicated chronic maladies the result of prolonged one-sided diets improperly followed or outlined, such as may be used in peptic ulcer, gastro-intestinal disorders, nephritis, epilepsy, and other conditions.

In the recent World War a disease called "*war edema*" was extensively studied on the Continent. It was the result of greatly restricted protein and practically starvation. Today a group of patients is seen clinically who present the picture of generalized edema, perhaps with secondary anemia, without cardiovascular renal disease, but who for varied reasons have been on a diet too low in protein and calories.

We have mentioned above that the American dietary is likely to be low in calcium. When this is combined with low Vitamin D or lessened activity of the parathyroid it may produce *tetany, osteomalacia,* or *dental caries.*

Diet plays a part of varying significance in many conditions and disorders (Tables 4-5) but the scope of this paper does not allow for their discussion.

CONCLUSIONS

Almost every physician has a different method and conception of dietetics. Most of these are variations of existing plans and "stock" diet-lists of greater or less antiquity and without the individual patient's consideration and needs. The many variations of dietotherapy make comparisons of results extremely unreliable. Because of the exploitation of pseudoscientists and the faddishness of the field of dietetics, there is a real need of placing emphasis upon the present scientific conception of the relation of nutrition to health and disease.

An attempt has been made briefly to touch upon the essential requirements that form the basis of an adequate and protective diet in health. In addition, outlines are presented to differentiate those diseases in which treatment by diet is of paramount importance and those conditions in which diet is of varying importance.

EARLIER VIEWS OF NUTRITION PROBLEMS*

Beaumont's Views on Digestion—Although food constitutes the chief item in the expense of living among the wage-earning class, and is more intimately concerned with the promotion of health and strength than are clothing, shelter and climate, it is only very recently that any serious thought has been given to the *nature* of food, and to the processes which it undergoes in being utilized for the bodily upkeep. Early man used the food he found available. Latitude, climate, soil and proximity to large bodies of water determined his dietary habits. Common observation showed that people in different regions of the world lived on diets of widely different character, yet without any markedly different success in physical development. Indifference to the nature of the food supply, with the exception of palatability, was therefore natural, since there was no obvious evidence that the character of the diet had anything to do with well-being.

The paucity of our knowledge concerning nutrition that existed toward the middle of the nineteenth century is well illustrated by the views expressed by Beaumont in his book "Physiology and Experiments", published about 1832. He had the good fortune to study the processes of digestion with the hunter, Alexis St. Martin, who had a fistulous opening into the stomach as the result of a gunshot wound. Beaumont collected gastric juice from his subject's stomach and studied its effect on various foods. He also introduced foods into the stomach and observed through the opening the behavior of this organ during digestion. He believed that the views of others to the effect that there were various kinds of nutrient substances were erroneous. In his opinion there was but one kind of food or "aliment" as he termed it. He believed this was present in all foods, and was simply dissolved out by the action of the gastric secretion. Beaumont was one of the most progressive investigators of his time. The chemistry of both inorganic and organic substances advanced with great rapidity during the nineteenth century. Among the facts which were established was that foods contained proteins, carbohydrates and fats, thus disproving the view that there was but "one kind of aliment". It is the oxidation of these food substances that yields the energy which keeps the body warm, and enables it to do mechanical work. The laws governing energy metabolism were next developed.

Lavoisier Placed Nutrition on Scientific Foundation—The modern era of the science of nutrition may be said to have been introduced by the famous French scientist, Lavoisier, in 1780. He was the first to apply the thermometer and the balance to the study of the chemical changes taking place in the living body. He established the fundamental fact that the production of heat involved the combination of the oxygen of the air with the substances taken into the body as food, and was in fact a process of combustion. He discovered that the temperature of the air had a pronounced influence on the rate at which substances in the body were oxidized. Oxidation is slow at temperatures which we find comfortable with light clothing, and is greatly accelerated by cold. He found exercise

* "The Newer Knowledge of Nutrition"—E. V. McCollum and Nina Simonds, The MacMillan Company, N. Y., 1925.

to stimulate combustion in the body, and he also observed that during work it might rise to several times the resting metabolism. These fundamental facts established by Lavoisier have formed the subjects of numerous investigations, which greatly increased our knowledge of detail in this important field.

About 1842 Joule described experimental data establishing the *mechanical equivalent of heat*. Heat is measured in terms of the small calorie, which is the amount of heat necessary to raise the temperature of 1 cc. of water 1 degree Centigrade. The calorie used in dietetics is the large or kilo calorie which represents the amount of heat required to raise 1 kilogram (2.2 pounds) of water 1 degree Centigrade or 1 pound of water approximately 4 degrees Fahrenheit. The rate at which energy metabolism varies with the activity of the individual, and in the absence of suitable clothing with the temperature, is the most spectacular phase of the metabolic processes. A man at rest may need about 1,600 calories a day in the form of suitable food, in order to cover his energy requirements. The same man at very severe labor requires 10,000 calories a day. It is not surprising that this obviously important phase of metabolism was early studied in great detail.

Studies on Energy Metabolism—Pettenkofer and Voit (1866) in Munich began the publication of their elaborate studies on energy metabolism. With the aid of a respiration calorimeter they measured accurately the amount of oxygen absorbed, the carbon dioxid and the water in the products of respiration, and the heat given off by the body under various conditions. They introduced into their experimental work the idea suggested by Liebig in 1842, viz., that the nitrogen eliminated in the urine could be made a measure of the amount of protein destroyed in metabolism, since protein is the one prominent food-stuff which contains this element. Pettenkofer and Voit studied the metabolism of fasting men and dogs, and of the same subjects when taking different kinds and amounts of food. From the magnitude of the "respiratory quotient", which is the figure obtained by dividing the volume of carbon dioxid eliminated by the volume of oxygen consumed in respiration $\frac{(CO_2)}{(O_2)}$ it was possible to decide what kind of food was being oxidized as a source of energy in the body. When carbohydrate is burned the quotient is 1. When fat is burned it is 0.7, and when protein is burned the figure is approximately 0.8. They found that a dog could be maintained in nitrogen and energy equilibrium during a period of a few days on a diet of protein alone (muscle tissue).

Specific Dynamic Action of Food-Stuffs—The early studies relating to energy metabolism led to the discovery that the protein of the food differs in one marked respect from either carbohydrate or fat, viz., its great stimulating effect upon metabolic processes as measured by the rate of oxidation. This is illustrated by the following type of experiment: if the rate of energy metabolism of a dog when it has been for some hours without food is carefully measured, it will be found that this remains constant within narrow limits so long as the animal remains at rest. If now it is fed liberally with either fat or carbohydrate and the observations on its energy metabolism are continued, there is observed a slight increase in metabolism which is the direct result of the utilization of these foods. If on the other hand, a liberal portion of protein-rich food, such as meat, is fed to the animal instead of the non-nitrogenous nutrients, there is a surprising acceleration of the metabolic processes, attended with a marked increase in energy set free within the tissues. This was first shown by Bidder and Schmidt in 1852. Their experimental animal was a cat. During a certain interval of time the animal used 50.18 gm. of oxygen and eliminated from its lungs 53.52 gm. of carbon dioxid. The animal was then allowed to eat all the meat it would consume and the observations continued. During a similar interval the cat used 103.84 gm. of oxygen and respired 113.52 gm. of carbon dioxid.

The remarkable researches of Voit, Pettenkofer, Rubner, Atwater, Lusk, Zuntz and Benedict on the metabolism of matter and energy in the body attracted deserved attention. For years this kind of study occupied a large area in the field of vision of students of nutrition. The researchers were extended to the study of some of the finer problems of metabolism. It was shown that carbohydrate can be converted into fat by the tissues, and that a part of the carbon which the protein molecule contains can be converted in the body into glucose. These investigations shed much light on such conditions of perverted metabolism as prevent the oxidation of sugar in the tissues (diabetes). In the light of the new developments in the chemistry of proteins and their digestion products, the amino-acids, Lusk finally explained in great measure the cause of the specific dynamic action of proteins (1915). Lusk (1922) says in the presence of an abundant quantity of oxidizable fragments of carbohydrate metabolism the heat production is raised to a high level. Definite affinities for carbohydrate consumption are satisfied which are not involved when the extra supply of glucose is being continually depleted under the regulatory control of the liver. The production of increased heat after carbohydrate ingestion may be termed the metabolism of carbohydrate plethora. The same conclusion is reached regarding fat as regarding carbohydrate: That in the presence of an amplitude of fat particles there is a metabolism of fat plethora due to the utilization of fat by special fat receptive cellular affinities. The specific dynamic action of protein consists in a specific chemical stimulus of the cellular protoplasm which is independent of the oxidation of the material through which the stimulus is applied. It may be termed the metabolism of amino-acid stimulation. A theory of metabolism is stated which is a modified form of one enunciated by Rubner: "One may conclude that the influence of food ingestion upon the basal metabolism of the quiet resting cell may be upon three independent mechanisms within the cells: (a) a mechanism which is receptive to a chemical stimulus derived from such amino-acids as glycine and alanine; (b) a mechanism of carbohydrate plethora which allows metabolism of carbohydrate up to certain limits imposed by self-regulation; (c) a mechanism capable of receiving power from that quota of fat which when in excess increases the heat production of the cell.

Section IV.

Roentgenology

Contributions by

WM. H. STEWART

WHY PEPTIC ULCERS ARE MISSED ON X-RAY EXAMINATION

By

WM. H. STEWART, M.D., *and* H. EARL ILLICK, M.D.

NEW YORK, N. Y.

IN THE last few years, progress has been made in x-ray examinations of the stomach and duodenum along the lines of investigating the morphology of the gastric and duodenal rugae and the pathological variations exhibited in peptic ulcer and malignancy.

Until recently, routine x-ray examination of the stomach and duodenum generally consisted of a varying number of films made in the erect, prone and oblique projections. Many hospitals or other laboratories with numerous gastro-intestinal examinations daily, follow a routine of fluoroscoping one patient after another, sending the cases into another room with directions to the technician as to the kind and number of films to be taken. The final result of such an examination demonstrates a large percentage of instances in which the films alone are inconclusive; not any exhibit a normal filling of the pyloric region or duodenal bulb. Either the roentgenologist's report must be based upon the fluoroscopic findings alone or the examination must be repeated or amplified. Spasm or other causes must be differentiated with certainty from organic disease and too often this cannot be done unless a prohibitive number of films is available for study and comparison or contrast.

A few words may not be amiss *concerning fluoroscopy.* The usual admonition is to use as little current as is consistent with clear visualization of the area under consideration. In stomach cases, the current necessary is much greater than in examinations of the chest or extremities and the common mistake is to have so little milliamperage that clear detail of the stomach, especially on the oblique views and in patients of large size, is not obtained. To miss pathology because one is unwilling to use enough current properly to illuminate the screen is an error.

Proper *protection* to the operator can be obtained by use of a completely protected tube of the most modern type and also a lead chair and proper gloves. Waiting long enough for adequate accommodation of the pupils, especially before fluoroscoping large size patients,—such details may seem too trivial to mention, yet experience proves that by not heeding such elementary rules ulcers frequently are missed. A fluoroscopic screen image should be sharp and definite enough to pick out an ulcer *niche* or crater on the posterior wall or else there is a serious defect in the technic. It may be necessary to use two or three times as much milliamperage or a much higher kilovoltage in order to penetrate certain patients sufficiently to be able to obtain clear definition of all parts of the anterior and posterior walls of the stomach and duodenal bulb in various oblique positions, yet if such lesions are not observed during fluoroscopy, it is very unlikely that films exposed in the usual manner, in standard positions, can possibly demonstrate them.

Occasionally it happens that considerable effort is spent watching a suspicious-appearing, duodenal bulb which never presents a characteristic defect from ulcer and yet never fills normally; closer scrutiny of the posterior wall of the *stomach* in a number of such cases, has demonstrated a large crater which was completely missed on the roentgenograms made in the usual oblique posture. In fact, one such case came to operation and the surgeon triumphantly demonstrated the huge crater although the films were negative. The crater was practically filled with a gelatinous, jelly-like material which probably prevented barium from entering the crater. Several times since then, we have had the experience of observing a stomach which appeared normal, but in which half an hour to an hour after the barium meal had been given, a crater was visualized. Such experiences make one reluctant hurriedly to examine stomach cases believing that, because the first few glances through the fluoroscope appear to demonstrate normal filling, therefore, no organic disease is present.

It cannot be too often stated that gastro-intestinal roentgen-study is time-consuming and that a few films, taken more or less haphazardly, may not constitute sufficient evidence from which to draw sound conclusions. Of late, special apparatus is necessary in order thoroughly to perform such a task in the best possible manner.

What constitutes the latest and best, proven method to examine the stomach and duodenum by means of the x-ray?

In addition to the time-proven methods of the past with which all are familiar, or should be, there are certain new methods which deserve trial and which give promise of aiding in the more certain diagnosis of lesions of the stomach and duodenum.

There has been a marked European trend in exerting every effort to study the gastric and duodenal mucosa, attempting to outline the rugae and to study patterns as they occur normally and in disease. The method holds much of promise when the effort is being made to distinguish malignant degeneration, especially around a gastric ulcer.

There is also increased interest in positively demonstrating the *niche* of a duodenal ulcer either for purposes of diagnosis or for study during the course of treatment.

The upper or the cardiac portions of the stomach are difficult to study with any mechanical means of exerting compression, but the pyloric half and the duodenal bulb lend themselves readily to such aids except when the stomach is of the high, transverse type.

A compressing device must be as thin as possible so that compression may be made and yet there will be no distortion due to the increased distance between the film and the stomach.

It is essential that one be able to fluoroscope and at any desired time immediately be able to switch over and obtain a radiograph of a certain filling. The apparatus now available may be adjusted for the proper roentgenographic setting before the patient is fluoroscoped and upon pressing a hand-switch an instantaneous exposure may be made at any time during the fluoroscopy, so that small films may be taken of any desired area.

A small apparatus is used to take the films which hangs upon the fluoroscopic screen of a vertical fluoroscope. The front of this apparatus is a compressor and any field may be selected through the fluoroscopic screen for detailed study. The apparatus is locked at this point and the area observed on the screen until a filling is obtained of the normal pre and post pyloric region or the lesion most favorably brought into view, at which time any number of exposures may be made. A magazine holds four small cassettes and one may be dropped at the second that the exposure is desired, the hand-switch closed and the exposure obtained. The cassette is then dropped into the lower magazine and the procedure repeated as desired.

The vertical fluoroscope must contain a tube which can take a radiographic-setting for stomach and duodenal work. The screen of the fluoroscope must be capable of

being locked into any desired position. The control of the x-ray machine must be set on fluoroscopy, but radiography must be possible by pressing a separate hand-switch. The serial-apparatus is worked with the other hand. Short practice makes it possible to obtain the films in a few seconds' time when the stomach is properly positioned and is functioning normally. The machine may be reloaded as often as desired. The small films permit considerable economy in what formerly were costly stomach examinations, and the results are superior to the older methods.

Many duodenal *niches* now are demonstrated which formerly were not visible on the films made *without compression*. The accurate positioning of the patient to bring out lesions accomplishes results not generally possible with the older and still more common procedures.

Patients with pyloric obstruction who come for examination with the stomach full of residue although no breakfast or fluids have been taken, must have the stomach emptied with a tube before the barium meal is given. Even then, it is sometimes impossible to demonstrate the exact morphology of the lesion responsible for the obstruction and to state whether it is benign or malignant but success is more sure when the gastric residue is at a minimum.

Gastric activity often subsides an hour after a meal. Films taken then are valueless. If the patient be given another glass of the meal renewed peristalsis is stimulated and emptying so that normal or diseased contours are possible to demonstrate.

The patient should be kept in the Roentgen department until films are developed and available for showing a suspected lesion or else a perfectly normal contour of the stomach and of the duodenal bulb. This may mean but one film but, again, twenty-five or more.

A polygraph by means of which four views are taken on one film is also a help in study of the pyloric region, when the patient is unable to stand.

COMMENTS

The *common causes for failure to demonstrate ulcer* or other organic disease in the gastro-intestinal tract may be summed up in one word: *haste*—hurry to get one case *through* and *out*, so that the next can be observed. Until *more time is taken mistakes will occur.*

Improved apparatus permitting radiography, *instantaneously, and during fluoroscopy* after patient has been properly positioned, is a great aid.

Study of the mucosa with compression is as essential as are the older full-distention methods.

FURTHER DETAILED DESCRIPTION OF THE SPECIAL COMPRESSION APPARATUS AND FLUOROSCOPIC ARRANGEMENT

The vertical fluoroscope used in the examination of patients for disorders of the gastro-intestinal tract is energized by a four-valve radiographic machine. On the control panel of this machine one sets the timer, autotransformer and filament for radiography of the patient before entering the room to begin fluoroscoping. When the foot switch is used, a fluoroscopic current energizes the screen. There is a hand-switch on the fluoroscope, by pressing which one obtains the radiographic exposure through the fluoroscopic tube at the setting previously determined. The screen may be locked in any desired position. The compression apparatus is hung on the frame of the fluoroscopic screen as illustrated.

In the top of this compression device four cassettes are placed. Fluoroscopy and localization of the desired area is obtained through the compressor in the center of the machine. When the ulcer is centered satisfactorily, a lever on the left side of the machine is moved and a cassette drops from the upper compartment down into the compressor. The patient is instructed to suspend respiration and the hand-switch is pressed so that a radiographic exposure is made. A lever on the right side of the machine is moved and the cassette drops down into the lower storage chamber.

This procedure may be repeated as frequently as desired. It permits instantaneous radiography of any desired area at any time while fluoroscoping.

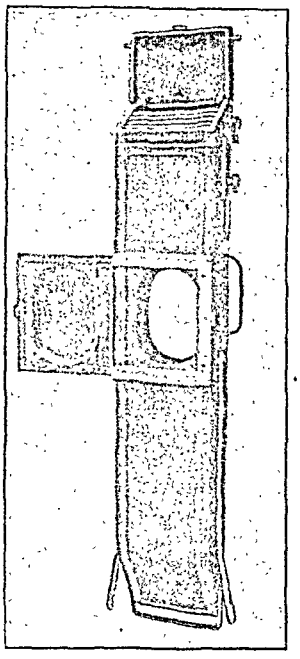


Fig. 1. Compression apparatus used to obtain instantaneous radiography during fluoroscopic examination.

Hinged top is open showing four cassettes ready for radiography.

The compressor is open demonstrating an empty middle chamber: in use, the compressor is swung back and this chamber is closed.

The levers for manipulating the cassettes are visible at the sides of the apparatus.

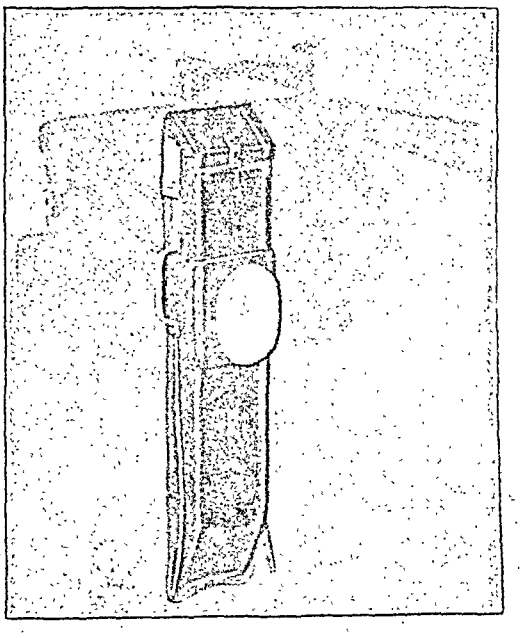


Fig. 2. Apparatus suspended on the frame of the fluoroscopic screen. The compressor is the white oval central area in the center of the illustration.



Fig. 3. An old-style prone roentgenogram demonstrates an apparently fairly normal filling of the duodenal bulb.



Fig. 4. An erect film of the same patient in which the niche of the duodenal ulcer is faintly distinguishable.



Fig. 5. Same patient: compression technique and correct arrangement of the patient to best demonstrate the lesion involving the posterior wall.

Figures 3, 4 and 5 show how the compression apparatus enables one to better demonstrate the lesion. With the ordinary technique the *niche* is barely discernable. By fluoroscopy with the compressor one may turn the patient until the lesion is most clearly demonstrated on the posterior wall and immediate roentgenograms are obtained for record.

Figures 6 to 11 (see page 55) represent six cases in which beautiful detail of the ulcer is brought out, the deformity and *niche* being demonstrated through the use of the compression technique.



Fig. 6.



Fig. 7.



Fig. 9.



Fig. 8.

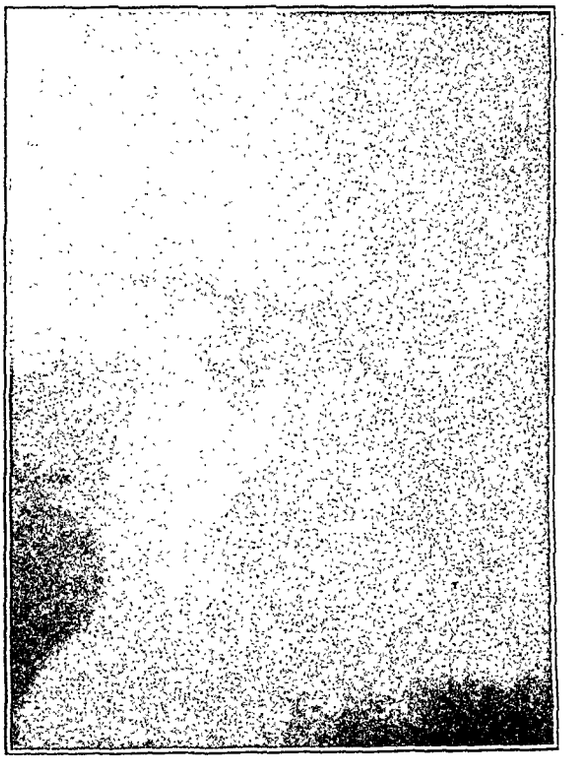


Fig. 10.



Fig. 11.

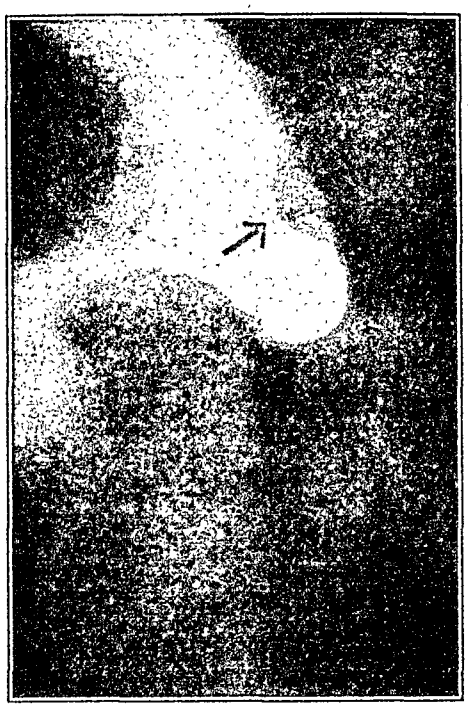


Fig. 12.

Figure 12 shows a gastric ulcer on the posterior wall of a type which if not located fluoroscopically is likely to be missed in routine roentgenograms. Such a crater may easily be overlooked fluoroscopically unless a thorough examination is made under ideal conditions. Turning this patient for half an inch either way was sufficient to cover this lesion completely. Sufficient fluoroscopic current must be used to render the posterior wall easily distinguishable when the patient is turned obliquely and the eyes must be well accommodated. This film was taken by means of a special compression apparatus which enabled the observer to make an immediate roentgenogram after localizing the lesion fluoroscopically.



Fig. 13.

Figure 13 represents a case in which there was a recurrence of ulceration after a sleeve resection for an original ulcer. This film shows the advantages of the compression technique in demonstrating the deformity, contracted rugae and the actual *niche*.

Section V.

Therapeutics

Contributions by

HORACE W. SOPER

TREATMENT OF AMEBIC DYSENTERY*

By

HORACE W. SOPER, M.D.
ST. LOUIS, MO.

OUR experience in the diagnosis and treatment of amebic dysentery is not entirely in accord with that described in the recent literature on the subject.

Some ten years ago, we had the opportunity of studying forty cases occurring in the celery fields in the vicinity of St. Louis. The workers were in the habit of eating the celery, as it was plucked, without washing it. In this epidemic, cysts of *endameba histolytica*, were demonstrable in a finely powdered manure that had been shipped from the South. All of these patients were seen early; soon after the symptom of diarrhoea had developed. Each patient was examined by means of the proctosigmoidoscope and invariably the early, superficial lesions were demonstrated in the rectum and in the pelvic colon. The lesions varied in size from one-tenth to one centimeter in diameter and were grayish-white in color, somewhat elevated above the surrounding mucosa. When gently swabbed with a small cotton-applicator, a very superficial ulcer was seen which oozed blood. The material removed by the swab consisted of viscid mucus, blood, pus cells, and numerous *endameba histolytica*. Large numbers of such lesions usually were seen, but some patients presented only a few. What we desire to emphasize is *that these ulcers invariably are present in every early case of amebic dysentery.*

Of course, in late cases, sedimentation of the feces, examination after a saline laxative, and other methods of diagnosis are indicated. While it is usually possible to demonstrate the ameba in feces-examination in the early stage of the disease, I have seen many cases in which the best laboratory technicians have failed to find them. *Therefore, a proctosigmoidoscopic examination should be made in every case of diarrhoea.*

During the treatment of the patients seen in the epidemic above referred to, finally there developed a standardized procedure of management. Briefly it was as follows: A daily dose of one grain emetine is given *intravenous* for seven consecutive days. Then follows the administration of one tablet of "stovarsol", three times daily before meals, for one week. Intravenous emetine is given once a week for a period of three weeks following the "stovarsol". In our cases the treatment in each case was ambulatory. Proctoscopic examination was made at each office visit.

The specific action of emetine perhaps is the most marvelous medicinal effect in the domain of therapeutics. After the third dose, motile organisms disappear from the rectal swab material. After the seventh day, the lesions have healed. No relapses occurred in the above series of cases. They were all followed for a minimum period of three months.

Since the experience gained in the above mentioned epidemic, we have seen thirty-five early cases—patients who had just returned from visits to the South. The same method of treatment was employed with equally good results. We had the opportunity to re-examine many of this later series of cases, months after the infestation, and no relapses have occurred.

Reed[1], Craig[2], Rogers[3], and others have warned against the indiscriminate use of emetine and advised that it be given subcutaneously. We have never observed a severe reaction from its exhibition intravenously. Some patients experience a feeling of giddiness and fulness in the head immediately after the injection of the drug. The initial dose should be given very slowly, and the patient should lie down for five minutes after each dose. The "stovarsol" and emetine should not be given at the same time. The great value of the daily intravenous dosage of emetine appears to be in the concentrated attack of the specific remedy on the ameba before secondary ulcers are formed, and before the protozoa get a chance to burrow deep into the bowel wall.

Most of the "carriers" that I have seen, have developed secondary ulcers in the *ampulla recti* just above the internal sphincter. A connective-tissue barrier forms which prevents emetine from reaching the ameba. In this class of patients, vigorous, local, proctoscopic treatment has given good results. The powder-insufflation method (using equal parts of bismuth subcarbonate and calomel through a powder blower) is of great value. The powder is soothing, non-irritant, and adheres tenaciously to the ulcerated area. The practice of using watery solutions as enemas or irrigations cannot be too strongly condemned. They produce irritation and congestion of the mucosa and invite further spread of the disease.

In conclusion, we wish to emphasize the importance of the proctoscopic method of diagnosis and to present an efficient, safe, reliable and routine method of treatment.

*From the Soper-Mills Clinic.

1. Reed, A. C.: *Am. Jour. Med. Sc.* 181:553 (Apr.) 1931.
2. Craig, C. F.: *Am. Jour. Trop. Med.* 8:29 (Jan.) 1931.
3. Rogers, L.: *Brit. M. J.* 1:1424 (June 12) 1912.

Section VI.

Abdominal Surgery

Contributions by

RALPH A. KORDENAT

PRIMARY CARCINOMA OF THE LIVER IN INFANCY*

REPORT OF AN INSTANCE

By
RALPH A. KORDENAT, M.D.
CHICAGO, ILL.

PRIMARY carcinoma of the liver is found in or after adult life in from 13 per cent to 28 per cent of all necropsies and observed so infrequently in childhood, that the case cited herewith seems worthy of report.

Rolleston[1] collected 32 cases under 10 years of age. Few instances are found in the literature of primary carcinoma in occurring under one year of age. Rolleston collected cases of Prescot (5 months); Ribbert (4 months); Peiper (8½ months); Wollstein and Mixsell (9 months); and two cases of Miller and Clelland (9 and 7 months). Milne[2] reported a simple liver-cell adenoma in a male child of 6 months. Eggel[3] mentions, among his collected cases, Pepper's case of an infant of 2 months. Rolleston has called attention to the fact that in older children portal cirrhosis with multiple adenoma very closely resembles carcinoma and undoubtedly many such cases were reported as being primary carcinoma. Others have called attention to the difficulty in orientating the reports of various observers and to the fact that different cases manifest individual peculiarities, making an accurate classification exceedingly difficult. The nomenclature is confusing. The descriptions of the appearances of different tumors vary with the observers.

Ewing's[4] classification of primary epithelial tumors of the liver based upon their histological morphology, seems satisfactory and presents an orderly-outlined list of hyperplastic growths, that previously lacked uniformity of description. It is quite generally recognized that primary, epithelial tumors of the liver arise from intra-hepatic ducts, or from both the liver cells and from the epithelial cells, lining the bile ducts.

Ewing classified epithelial hyperplasia and tumors of the liver as follows:

1—SIMPLE HYPERTROPHY AND HYPERPLASIA
- A—Regeneration
- B—Congenital
- C—Nodular Hyperplasia in Stasis or Cirrhosis
- D—Diffuse Hyperplasia (Diabetes)

2—NEOPLASTIC HYPERPLASIA
- A—Hepatoma
 - 1—Adenoma
 - 2—Adenocarcinoma
 - 3—Carcinoma—Solitary, Multiple or Atypical
- B—Cholangioma
 - 1—Adenoma—solid or cystic
 - 2—Adenocarcinoma
 - 3—Carcinoma
- C—Mixed Tumors

In considering the general etiology of all primary carcinomata of liver, we have precious few positive facts. They usually occur after 40 years of age and rarely in infancy. There is no uniform data as to sex.

Various opinions have been expressed relative to the actual cause. Ewing believes that congenital maladjustment of liver cells predisposes to tumor growth, yet believes this to be a rare factor in adults—while of most importance in infants. Watzold (quoted by Milne) suggested irritation of the liver as a possible cause. Klob and Wagner found isolated accessory nodules of liver tissue in the suspensory ligament and from this argued that such misplaced portions of liver tissue are capable of tumor production. It has been suggested that if foetal misplacement of liver tissues has occurred, it must have happened at a stage when liver cells are differentiated, while in these growths only one type of cell is in evidence. It seems reasonable to suppose, however, that Ribbert's theory may explain the cause of these tumors of infancy. He believes that the basis of tumor growth is the independence of a tissue germ attained through isolation of the cell. Isolated cells, pinched off in embryonic development, must have an adequate capacity for growth, though they may not form tumors unless their environment is highly favorable to their development. It would be reasonable to suppose that if every group of cells, isolated during the very early embryonic development, would develop into tumors—cancerous or otherwise—all animal life soon would cease. Such misplaced cells must have proper nutrition and a favorable chemical and physical environment, together with other factors, expressed by MacCallum as "irritation" or other injurious influences that disturb normal growth of tissue. MacCallum has called attention to the fact that there are very definite laws of normal growth from the beginning to the end of life, and that tumor growth does not obey these laws, but transgresses them in every direction. Embryonic cells may explain the growth of teratoma but not of tumor growth. It seems that, in addition to injury and irritation, etc., there must be some unrecognized, sudden and profound abnormality of the cells themselves that induce tumor formation. In the instance here recorded, there was a very definite history of a rather prolonged gastro-intestinal upset, probably secondary to faulty feeding, that may have supplied through the portal circulation, irritative substances to the liver cells, misplaced or otherwise, favoring the neoplastic reproduction of the cells. There seems to be no conclusive evidence relative to the parasitic origin of primary carcinoma of the liver.

PATHOLOGICAL DEVELOPMENT

Pepell (quoted by Ewing) has described supra-renal "rests" in the liver—yet carcinoma could hardly be due to adrenal tissue, inasmuch as the cells of many carcinomatous tumors have been seen to mimic the parent tissue by secretion of bile. Bile and fat granules are seen in the cells in some instances.

A large group of observers consider simple adenoma as a sequel to compensatory hyperplastic changes and, not a few observers, emphasize very strongly the close association of cirrhosis as a possible etiological factor. Cirrhosis, and the factors that lead toward it, cause degeneration followed by regenerative overgrowth which may become excessive and neoplastic. Such factors seem unlikely, however, in infancy. Displaced lobules of liver-tissue have been described within Glissen's capsule and scattered throughout the peritoneum. These are considered by some as a favorable argument for the congenital origin of cancers of the liver.

Ewing[4] believes that there is a uniform gradation between nodular hyperplasia, multiple adenoma and carcinoma, and they may be observed in the same liver. Though there may be a sudden transformation between hyperplastic and neoplastic cells during this transformation, the cells may retain their granular character of liver cells, but stain more intensely with basic dyes or they may lose granules and pigment and may assume the transparent character of embryonic cells. Bile secretion is said to diminish with hyperplasia. The nuclear hypertrophy and hyperchromatism are constant and multinucleated and giant-cells appear. Mitosis is frequent as is seen in the photograph illustrating our case. The change in the nuclei of neighboring liver cells, a feature of collateral hyperplasia was not noticeable in the instance here recorded. The entire right lobe was composed of tumor tissue, while the left lobe showed the changes seen in the extreme passive con-

*From the Department of Surgery, College of Medicine, University of Illinois

gestion. Early generations of the tumor cells were observed by Ewing to be large, while later the cells are small and atypical. A marked preservation of new growth of capillaries has been observed by Ewing and this may reach an excessive state in the "angioplastic pseudo-sarcomas". Milne, Rolleston, Ewing and others have demonstrated the proliferating epithelium of the bile ducts in the cirrhotic livers.

The histogenesis of the mixed types is not clear, though these occur usually in cirrhotic livers. It is quite possible that the cells, resembling liver tissue in such cancers, are cells which have differentiated from cells growing centripetally from the bile ducts in a manner similar to the growth of such cells during normal regenerative processes as shown by MacCullum.

Metastases occur very early as an invasion of the capillaries. Such loose, intra-vascular thrombi have been recorded to appear in relatively benign tumors and from secondary nodules through the liver. From such tumors thrombi may extend into the *vena cava*. Metastases elsewhere, however, are not great, though they have been reported in the lymph nodes, lung, colon, pancreas, ovary and thyroid.

The *clinical course of primary tumors of the liver* is not long after the tumor mass has been noted; seldom more than 4 months. Fever is observed due to the rapidly growing tumor and infection, and occurs in 14 per cent of the cases. (4) Jaundice occurs in 61 per cent and ascites in 58 per cent of the cases. In a large number of the cases, the patient dies suddenly from hemorrhage after an illness of a few days. In some cases, primary carcinoma of the liver is found at post-mortem examination of patients, who died of cirrhosis of the liver. There is another group where there is the usual history of cirrhosis terminating suddenly with hepatic tumor, jaundice, ascites and cachexia. In still another group, there is the usual history of a malignant tumor, pointing from the first to the liver, developing in a previously healthy subject. Ewing quotes Keen and Yeomans, who successfully excised a carcinoma, but ordinarily recovery is unlooked for.

Ewing has classified anatomically the following varieties of carcinoma of the liver:—

Hepatoma—A—Solitary Liver Celled Adenoma. Solitary liver celled adenomata appearing in early life—3 months and later, hence are often regarded as congenital in origin. The solitary adenoma is gray-yellow or bile stained. It is encapsulated, varying in size from a small nodule to a mass 8 inches in diameter. The tumor is composed of cords, tubes and alveoli, resembling liver structure. The cells, though, are granular and acidophilic or fatty. The stroma consists chiefly of capillaries. The cells often secrete bile. The veins are not invaded. The benign character is due to encapsulation. The transition to the stage of adenocarcinoma is manifest by the invasion of the veins and the multiplication of the tumors.

B—*Primary Massive Liver Celled Carcinoma* occurs in young adults, but more often in aged. It is accompanied by cirrhosis. There are no symptoms, except those due to cirrhosis until a brief terminal period. The tumor appears as a large, single yellowish mass—soft. Liquefaction necrosis produces a cystic appearance; the veins usually invaded result in lung metastasis. The structure is variable, but always reveals at some point definite resemblances to liver cells. This is a rapidly growing atypical and malignant form of solitary adenoma.

C—*Multiple Liver Celled Carcinoma.* This group includes highly malignant rapidly growing tumors, occurring in livers in which cirrhosis is either absent or so slight as to be of secondary importance. No sharp division between this group and solitary massive carcinoma—and multiple carcinoma, following cirrhosis. The clinical course is rapid, usually a few weeks. Jaundice is uncommon, but a bloody serous effusion has been observed. There is rapid cachexia and enlargement of the liver with ascites. The liver is tremendously enlarged, multiple nodules, grayish or hemorrhagic in appearance. It is hard to decide which is the primary tumor. There are no metastases. Most tumors yielding metastases are associated with cirrhosis. In these one finds small alveoli and numerous capillaries. There is no definite encapsulation.

D—*Carcinomatous Cirrhosis—Hepatoma and Cirrhosis—Carcinoma—Multiple Adenoma.* Here there are progressive invasion and malignant tendencies with cirrhosis. It usually developes in elderly people. The liver is usually contracted, the surface presents multiple nodular bile stained nodules. Ascites, cachexia and various hemorrhages are the rule.

CASE REPORT

BABY JAMES T.—Age 11 months, was admitted to St. Joseph's Hospital, Chicago, at 7 P. M. on Dec. 29th, 1933. The mother stated that the infant became ill at 2 o'clock that afternoon, with apparent abdominal distress and fever, and that a "lump" appeared at this time in the right upper abdominal quadrant. There had been no bowel movement since that noon. There was no vomiting. The infant had not been normal for the preceding three weeks, during which time the child had "frequent colds". Stools were then frequent, stringy and green, though there was no bleeding.

Physical examination revealed a fairly well nourished, well developed male infant for 11 month, but who appeared anaemic and in pain. He cried incessantly. There was a large freely movable mass in the right upper abdominal quadrant; quite firm in consistency. A satisfactory examination was difficult. There was no visible peristalsis. The abdomen was rigid. The leucocyte count was 20,000.

An *exploratory laparotomy* was done. A tremendously enlarged liver was found with presentation of its inferior surface. In the midportion of the inferior surface, was a soft, circular, bulging area about 10 cm. in diameter. A trochar was inserted in this bulging mass and nothing but blood withdrawn. Bleeding was excessive. Suturing of the liver was attempted to control the bleeding without much success. The abdomen was closed with a small gauze pad pressing against the bleeding surface of the liver. The infant died the following morning. A necropsy was performed by Dr. L. E. Hines, whose findings were as follows:—

AUTOPSY REPORT

DESCRIPTION: The body of the infant weighed 8 kilograms. The skin was generally pale. The fontanelles were closed. The sclerae and conjunctivae were white and very pale. There were four upper and four lower incisors present. There were palpable lymph nodes in the angle of the jaw on both sides. There were patches of subcutaneous ecchymoses on the right hand and the dorsal surface of the right forearm. There were excoriations of the left buttock and both thighs. The testes were in the scrotum.

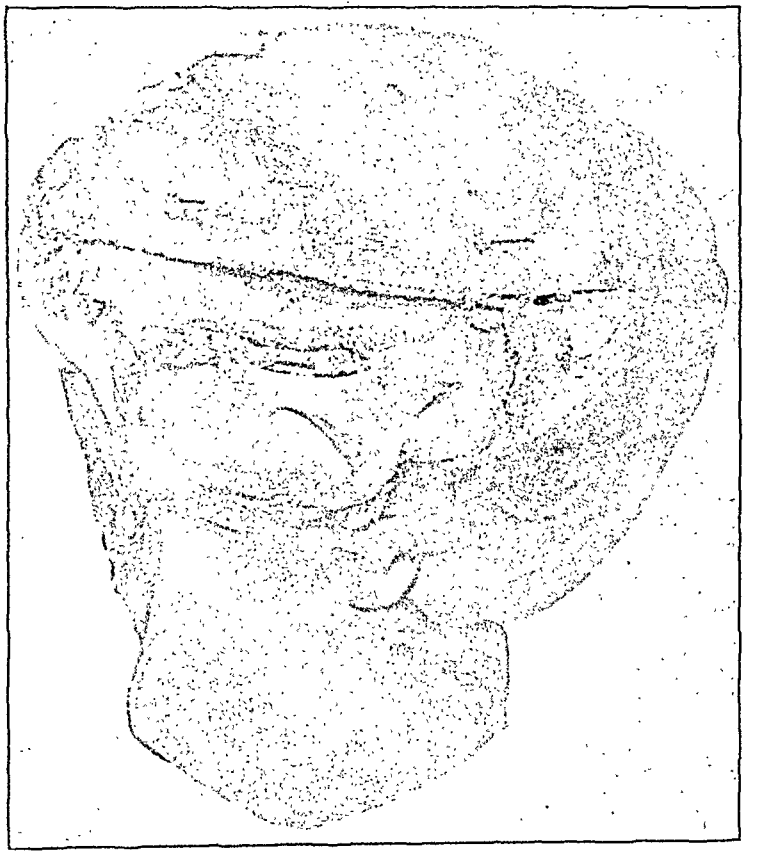


Fig. 1—Primary Carcinoma of Liver; inferior surface, showing involvement of entire right lobe. Incision was made at post mortem. Normal gall bladder is shown with fundus removed.

The fat in the midline was 1 to 2 cm. thick and very pale. The umbilical vein was closed. The liver was huge, measuring about 19x22 cm. and occupied about three-fourths of the abdominal cavity, extending 11 cm. below the costal margin in the mid-clavicular line. It occupied the entire epigastrium and extended 9 cm. below the xiphoid. The spleen was free. There were no adhesions between the dome of the liver and the diaphragm. On the inferior surface of the liver, there was a blood clot adjoining a puncture wound (made during operation). There was also a sutured incision on the anterior surface of the liver near the lower border. The entire colon was crowded to the left side of the abdomen. The lesser omental sac was free. The appendix was normal. The lymph nodes of the mesentery were enlarged and very firm.

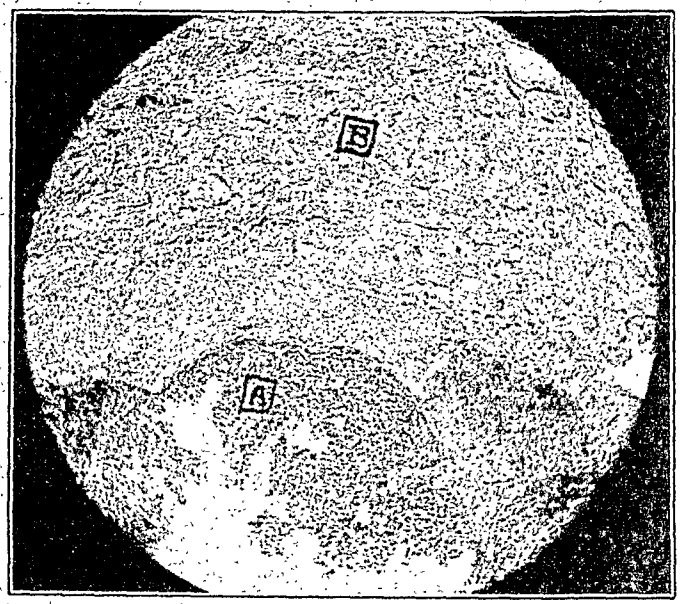


Fig. 2—Primary Carcinoma of Liver; showing margin of main tumor mass with attempted encapsulation and extension of narrow epithelial strands.

Both pleural cavities were free. The thymus gland weighed 18 cm. and was without gross changes. The pericardial sac was free and there was no excess fluid. The lining of the inferior *vena cava* was smooth. The lining of the aorta was smooth and contained only fluid blood. There was no change in the trachea, and no enlargement of the periaortal, peritracheal or peribronchial lymph nodes.

The lungs were very pale. The pleural surfaces of both lungs were smooth. There were no changes of the cut surfaces of the lungs.

The heart was about normal in size. There was slight distention of the right atrium. The *foramen ovale* was closed. There were no changes of the tricuspid, pulmonary, aortic or mitral valves. The interventricular septum was intact. The heart muscle was firm and pale.

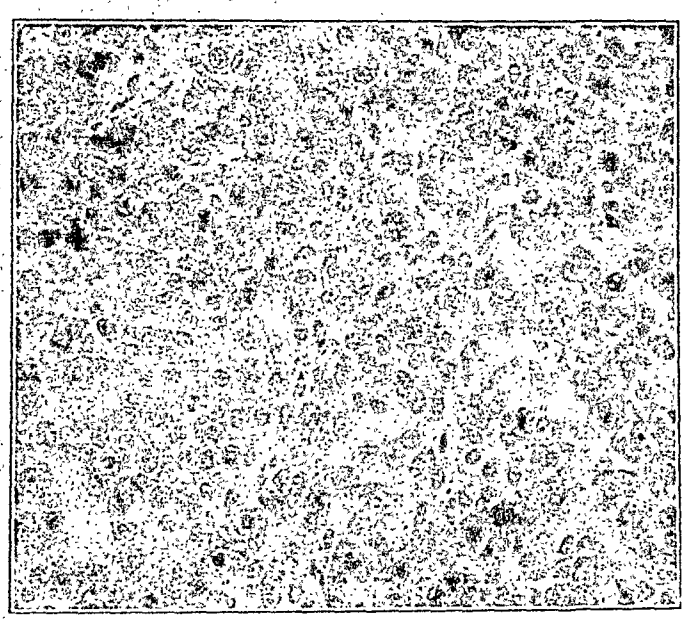


Fig. 3—Primary Carcinoma of Liver; Point A in Fig. 2, showing roughly arranged immature cells, some of them resembling liver cells, with granular cytoplasm.

The enlargement of the liver was entirely in the right lobe. The surface was somewhat nodular, the nodes were light yellow to grey and the intervening liver substance was a reddish brown color. Almost the entire right lobe was replaced by a soft, light grey, nodular tumor mass. Scattered throughout the tumor substance, there were purple areas which faded into adjacent liver substance. The substance of the tumor was very friable. There was some scar tissue between the lobules. There was no tumor invasion of the left lobe and no extension through the liver capsule. The gall bladder contained yellow bile. The wall of the gall bladder was thin, the lining was smooth. The liver weighed 1120 gms. There were no changes of the principal bile ducts.

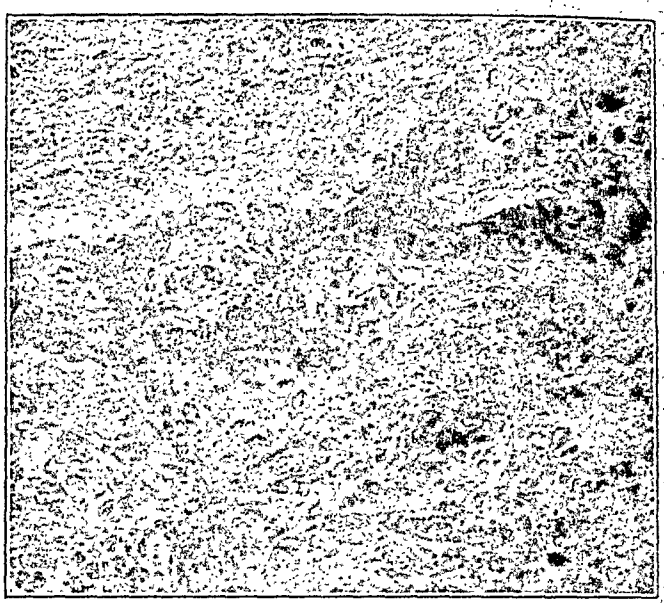


Fig. 4—Primary Carcinoma of Liver. Point B in Fig. 2, showing narrow epithelial strands within the dense fibrous tissue.

The kidneys were about normal in size. Fetal lobation markings were still present. The capsules stripped easily, leaving smooth surfaces. The kidney substances were firm. There were no changes in the urinary pelves and no evidence of tumor infiltration.

The spleen was about normal in size, weighing 50 gms. The splenic substance was very firm and pale. Surfaces made by cutting were pale.

The lining of the stomach showed prominent rugae, without ulcerations or tumor masses.

Multiple sections of the pancreas, testes and small intestines showed no abnormalties.

ANATOMICAL DIAGNOSIS: Primary solitary liver cell carcinoma of the right lobe of the liver; marked generalized anaemia; recent surgical abdominal incision and surgical exploration wounds of the liver.

MICROSCOPIC: Between normal liver tissue and tumor there is a zone in which the liver parenchyma is hemorrhagic. In the tumor are found two types of structure: sharply circumscribed areas of cellular tissue with immature cells roughly arranged like parenchyma cells of liver—many mitotic figures present; the other type is composed of narrow epithelial strands separated by dense fibrous tissue.

SUMMARY

A case of Primary Solitary Liver Carcinoma is reported in a male infant 11 months of age.

Complete autopsy findings are presented.

A review of the literature concerned with primary liver malignancy has been made. Theories of the mechanism of production and the locations of origin of primary liver tumors are discussed.

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ABSTRACTS

WANGENSTEEN, O. H. AND PAIN, J. R.

"Treatment of Acute Intestinal Obstruction by Suction with the Duodenal Tube." Journal A.M.A., November 11, 1933, Page 1532.

The authors believe their results warrant a change in the established management of the simple intestinal obstruction case. They observed that acute intestinal obstruction from adhesions was often permanently relieved by enterostomy and the continuity of the bowel re-established by the decompression. They accordingly used the duodenal intubation of Levin and carried out continuous suction siphonage with the simple apparatus of an inverted water bottle. They demonstrated that the small intestine readily could be decompressed in this way, obstruction relieved and toxemia controlled. X-ray demonstrated gas passing freely into the colon. In cases where the obstruction was not relieved and when operation later became necessary, the patient was markedly improved as an operative risk. Obviously, strangulation is an indication for immediate operation. Obstruction in the descending colon likewise is not usually amenable to decompression especially where there is marked distension of the proximal colon and angulation at the ileocolic sphincter.

Loud intestinal *borborygmi*, heard with the stethoscope at the acme of intermittent crampy pain, are useful in following intestinal obstruction, together with X-ray films of intestinal dilatation. Vomiting is a prominent symptom but in simple obstruction the general condition of the patient is not disturbed until later in the course of the obstruction. Diminution of the plasma chlorides, elevation of the non-protein nitrogen in the blood and alkalosis occur consistently, in only high obstruction and then only after persistent vomiting of about 48 hours duration. Strangulation is suggested by quickening of the pulse, leukocytosis, and elevation of temperature.

The Levin tube, even when held within the stomach, decompresses the small intestine to a certain extent through the pylorus. It is better, of course, if it passes into the duodenum. The authors have made it routine practice to cut extra holes in the duodenal tube as far back at ten inches so there may be simultaneous suction in both stomach and intestinal canal. Emptying the stomach by suction aids the tube's passage into the duodenum as also do inhalation of amyl nitrite which relax the pyloric sphincter. The use of a special weighted tip on the tube is recommended. The presence of both gas and fluid prevents a too rapid decompression. Segments filled with gas and fluid are alternately and therefore slowly decompressed. The authors found that a suction of 75 centimeters of water to be of optimum value. Pain and distention are very satisfactorily controlled and the patient is greatly relieved. The decompression can be followed by X-ray films as the final test. Narcotics are best avoided but hot packs are used over the abdomen. Fluids are given by infusions: 3,000 to 5,000 cc. of dextrose in physiologic salt solution being given by the slow drip method.

The authors treated thirty-two cases in the manner described. Only nine were operated upon. Twenty cases of obstruction were treated by decompression by suction alone. In this group, there were three deaths, two of which occurred sometime after decompression, due to cause unrelated to the obstruction. Only one death was directly attributed to the obstruction of the bowel by a gall stone, in which operation should have been done.

Ordinarily satisfactory and complete decompression was achieved only after 48 hours or more but the toxemia was then regularly decreased and the patient's general condition improved. Obstruction of the bowel proximal to the splenic flexure therefore no longer presents an acute emergency demanding immediate operation except in frank strangulation.

V. C. Rowland.

MILES, W. ERNEST.

"Recto-sigmoidectomy as a Method of Treatment for Procidentia Recti." Proc. Roy. Soc. of Med., 26:1445-1448, Sept. 1933.

Thirty-one cases were operated upon by this method with one death, not directly due to the operation. The end-results were remarkably good. There was one case of recurrence which occurred 5 years after the primary operation. The prolapse was resected, and the portion of the pelvic colon which was removed contained eleven diverticula, each of which contained a mass of faeces. Sphincteric control gradually improves, and at the end of six months or less is usually fully restored. Much, however, depends upon the assiduity with which the patient carries out the instructions given in regard to practising contraction of the sphincters at intervals during the period of convalescence.

F. D. R.

DANIEL, WILLIAM H.

"Rectal Diseases—Their Injection Treatment." Calif. and West. Med., 40:85-88, Feb., 1934.

Internal hemorrhoids of the simple bleeding or prolapsing type, constituting probably less than 40 per cent of rectal conditions, respond most readily to injection treatment. This treatment has an important place in that group of patients with constitutional disease, in the aged, for whom any type of surgery is dangerous, and for those individuals who refuse any kind of operation. Successful treatment by this method with a minimum expense and loss of time may encourage others to seek advice so that lesions may be eradicated before they become dangerous. On the other hand, Daniel warns that the improper application of this treatment will bring it into disrepute. Wrong diagnosis is as often at fault as mistreatment. Conditions mistaken for internal hemorrhoids are: anal fissure or ulcer, external thrombotic hemorrhoids and skin tags, abscesses, chronic ulcerative proctitis and colitis, amebic proctitis, cryptitis and papillitis, pruritus, benign tumors, carcinoma of rectum and sigmoid, genito-urinary diseases, and disorders of the female pelvis.

C. L. L.

STEINBERG, MOSES E.

"The factor of spasm in the etiology of peptic ulcerations." West. J. Surg. Obst. & Gynec., 41:663-670, Dec., 1933.

Experiments on dogs were carried out which indicate that spasm is an important factor in the etiology of peptic ulcerations. Chronic ulcers of the jejunum occurred with regularity when the alkaline duodenal contents were diverted from the gastrojejunal anastomosis according to the method of Exalto. When the muscle layers were stripped in the jejunal wall anastomosed to the stomach, no ulcers took place in the mucosa where the muscle layers were stripped. Exactly where muscle layers began an intact course, or about ten centimeters from the gastrojejunal anastomosis, chronic ulcers were found in several animals.

M. L. F.

PEMBERTON, JOHN DEJ. AND DIXON, C. F.

"Summary of the End-Results of Treatment of Malignancy of the Thyroid Gland and the Colon, Including the Rectum and Anus." Surg., Gynec., & Obst., 58:462-464, Feb., 1934.

Of the 3,542 cases of malignancy of the colon and rectum, operated on at the Mayo Clinic between January 1, 1907, and July 1, 1924, 28.14 per cent survived for five years or longer. Prognosis following operation is best if the growth is situated in the proximal or right portion of the colon and becomes less favorable as the growth becomes more distant from the right side. In 57 cases of the cecum the percentage of 5-year survivals was 51.81 per cent; colon, 144 cases, 48.97 per cent; sigmoid, 109 cases, 40.67 per cent; recto-sigmoid, 116 cases, 36.94 per cent; rectum, 347 cases, 35.88 per cent; anus, 3 cases, 42.85 per cent. In approximately two-thirds of the cases, the growths were in position to be palpated by the index finger if a careful rectal examination were made. About 25 per cent of the patients suffering from such malignancies are operated on for haemorrhoids before the lesion producing the symptoms is identified. If malignancy of the colon and rectum is to be detected in its early stages, digital examination of the rectum should be routine, and proctoscopic and roentgenologic studies of the colon should be included in the examination of all patients with intestinal complaints of indeterminate nature.

C. C. O.

COFFEY, ROBERT C.

"Cancer of the Rectum." Surg., Gynec., & Obst., 58:465-467, Feb., 1934.

From this study, including 239 cases of carcinoma of the rectum and rectosigmoid, it would appear that from the radical abdominoperineal operation in two stages one may expect an operability of approximately 50 per cent, operative mortality of approximately 10 per cent, and of those recovering from operation approximately 50 per cent of 5-year cures. In a given number of cases of carcinoma of the rectum it seems certain that a larger number of 5-year cures may be obtained by the abdominoperineal operation in one or two stages than by any other method.

W. J. J.

ABBOTT, W. OSLER.

"Acetyl-B-Methylcholin. Its Action on the Gastro-Intestinal Tract of Normal Persons, in Abdominal Distention, and in Certain Other Conditions." Am. J. Med. Sc., 186:323-330 Sept., 1933.

Animal experimentation, special studies in normal individuals and clinical use has proved that motor stimulation as evidenced by in-

crease in tone and peristalsis is the chief gastro-intestinal effect of acetyl-B-methylcholin, though secretory activity of the stomach may be at times increased.

This effect is most satisfactorily achieved by oral administration, secretory and cardiovascular activity dominating the picture after subcutaneous injection.

Beneficial clinical effects have been manifested by slight stimulation of gastric secretion in some cases of hypochlorhydria, by a comfortable laxative effect in most individuals taking large doses by mouth, but chiefly in the relief of abdominal distention in certain instances in which the usual procedures had failed.

J. S.

ROSS, LLOYD I. AND JOHN M. TOMASCH.

"Hyperinsulinemia secondary to an adenoma of the pancreas." Arch. Surg., 28:223-231, Feb., 1934.

In the case reported the onset was abrupt with complete loss of consciousness and evidence of external injury, that caused the patient's symptoms to be attributed to cerebral edema or concussion. Excision of a small pancreatic nodule restored normal carbohydrate metabolism and there were no further seizures of hypoglycemia. Additional evidence is afforded that in some instances a tumor arising from glandular tissue may retain the function of the organ or tissue from which it arose. Exploration and removal of the tumor offers the best chance of clinical cure. The patient presented the semi-Babinski or extensor response noted by Hart and Bond as a diagnostic aid in differentiating between insulin shock and diabetic coma.

J. S.

CARLSON, HJALMAR E. AND THOMAS G. ORR.

"Experimental obstruction of jejunum." Arch. Surg., 28:292-295, Feb., 1934.

These experimental findings suggest that continuous lavage of the stomach in acute intestinal obstruction is beneficial. The upper part of the jejunum was obstructed in twelve healthy adult dogs six of whom were deprived of food and water while the remaining six were deprived of food but given water freely. Those deprived of water showed relatively little change in the blood chlorides, carbon dioxide-combining power and sugar compared to the animals receiving water. The animals showing greater change in the chemical composition of the blood lived longer than those showing little change and the loss in body weight was slower. Water absorbed from the upper gastro-intestinal tract, apparently, helped to prolong the lives of the dogs.

F. G. O.

BAUER, GUNNAR.

"Zur Behandlung der Appendicitis—Peritonitis. (Treatment of Appendicitis — Peritonitis.") Acta Chirurgica Scandinavica, 1933 Vol. LXX., Supplementum XXIV. 461 Pages.

This clinical study, covering all the appendicitis cases treated at the General Hospital, Malmo, from 1896 to 1930, in all 6,218 cases, concerns chiefly the treatment of the different varieties of appendicitis-peritonitis and complications, especially post operative ileus.

From and including the year of 1903, when the therapeutic principles became stabilized and patients began to reach the hospital in a fairly favorable stage, 5977 cases of appendicitis were treated, with 176 deaths and a mortality of 2.9 per cent. Of these cases, 769 (12.9 per cent) were chronic and 5208 (87.1 per cent) acute. Among the former there were two (2) deaths (mortality 0.26 per cent) among the latter 174 (mortality 3.3 per cent).

In 569 cases of appendicitis with noncircumscribed peritonitis (1909-1930) the majority of which were treated by immediate suture, the mortality was 10.7 per cent. In 676 cases of circumscribed peritonitis (1903-1930), the majority of which was treated by immediate and radical operations the mortality was 6.9 per cent.

An entire chapter is devoted to the non-circumscribed form to determine the advisability of immediate operation and immediate closure of the abdominal cavity. A number of experimental investigations and theoretical considerations are adduced which appear to show that drainage of the abdominal cavity is an impossibility.

The Malmo material is presented as representative of results of immediate operation and immediate suture. The author concludes that the dangers of the expectant treatment are too grave. The mortality rate and healing conditions in cases of immediate suture are presented "as very favorable" when compared with those in drained material, and similarly the length of stay in the hospital for cases treated according to the immediate suturing method was extremely short, on an average, only 25 days.

The most gentle treatment of the peritoneum is observed and with such care, irrigation or mopping up of the exudate in the abdomen have an equal advantage. An adverse stand is taken in regard to infusion of fluids or other agents into the abdominal cavity. Lymphaticostomy is condemned. Serotherapy seems "highly desirable". In general treatment the administration of sodium chloride solution in large quantities, parenterally or by rectum, plays a decisive part. The importance of maintaining intestinal peristalsis is emphasized and to this end "scarcely any measure ought to be left untried."

In a purely paralytic ileus once established only such agents as act directly upon the intestinal musculature or its nervous apparatus can be of real benefit, e. g. the hypodermically injectible purgatives as well as intravenously injected hypertonic sodium chloride solutions, splanchnic or spinal anaesthesia, and, once again, serotherapy, in addition to which a drainage of the stomach is always of value.

In a similar study of the therapy of circumscribed peritonitis the conclusion is reached that the prompt, radical procedure shows the lowest mortality in cases having a duration of illness of up to and including 5 days and this also in cases having a palpable mass, whereas the more advanced cases show the most favourable mortality under conservative treatment.

W. S. Z.

DRAGSTEDT, LESTER R., H. E. HAYMOND AND JAMES C. ELLIS.

"Pathogenesis of acute pancreatitis (acute pancreatic necrosis)," Arch. Surg., 28:232-291, Feb., 1934.

In an extensive study combining experimental and clinical findings and a review of the literature (bibliography appended), conclusions are reached concerning the pathogenesis of pancreatic necrosis which have a bearing on treatment. The trial of B. welchii antitoxin appears to be justified by the almost regular finding of this organism in the necrotic pancreas in the animal experiments. The exact nature of the poison responsible for the toxemia, being still unknown, attempts at treatment are practically limited to preventing the entrance of additional poisons into the blood stream. Since in all probability the majority of the cases are due to the passage of bile into the pancreatic ducts, it seems wise to reduce the pressure in the biliary tract, diverting the bile, and possibly the pancreatic juice, to the exterior by means of cholecystotomy or choledochostomy. A negative pressure bottle might well be connected with the drainage tube. Local is probably safer than general anesthesia because of the susceptibility of etherized animals to histamine. Drains may be placed about the pancreas to facilitate the formation of adhesions and the isolation of the pancreas. The intravenous administration of physiologic solution of sodium chloride or Ringer's solution is advisable to correct the alterations in blood chemistry and the dehydration accompanying paralytic ileus. Possibly parenteral administration of large amounts of salt solution may facilitate the excretion of soluble toxic chemicals from the blood stream. Repeated gastric aspirations prevent overdistention and help to restore stomach tonus.

It is probable that about 60 per cent of the cases of acute pancreatic necrosis in man arise in patients with antecedent chronic biliary tract disease and that the immediate cause of necrosis is the destructive action of the bile in the pancreatic ducts. The amount of pancreatic juice present in the necrotic pancreas is insufficient to account for the toxic effect. However, the digestion of the protective proteins of blood serum by the proteolytic enzymes of the pancreatic juice frees the bile salts for further destructive action, and this probably accounts for the greater susceptibility of the pancreas to biliary necrosis than is found in other glandular organs.

D. C. S.

Section VII.

Surgery of the Lower Colon and Rectum

Contributions by

JEROME M. LYNCH
LOUIS A. BUIE
CLEMENT L. MARTIN

UNUSUAL PROBLEMS IN PLASTIC SURGERY OF THE COLON

By

JEROME M. LYNCH, M.D., F.A.C.S.

VINCENT HURLEY, M.D., F.R.C.S. (Eng.)

NEW YORK, N. Y.

Twenty-five years ago, Sir Frederick Treves, sergeant surgeon to King Edward the Seventh, surgeon to the London Hospital, famed writer and teacher, leader of English surgery and still in his fifties, suddenly announced his retirement. "Surgery had become standardized", "stale, flat and unprofitable", "only minor technical advances were possible". Yet Sir Victor Horsley had just removed the first spinal cord tumor, the thorax was still almost closed, the surgery of the genito-urinary system was awaiting the development of the X-ray, the cystoscope and the opaque media. Heroic and multilating operations were being done in the mouth, tongue, jaws and neck—a field now almost entirely surrendered to radiotherapy, electro-therapy and the actual cautery. Truly will the surgeon continue falsely to prophesy that the bourne has been reached.

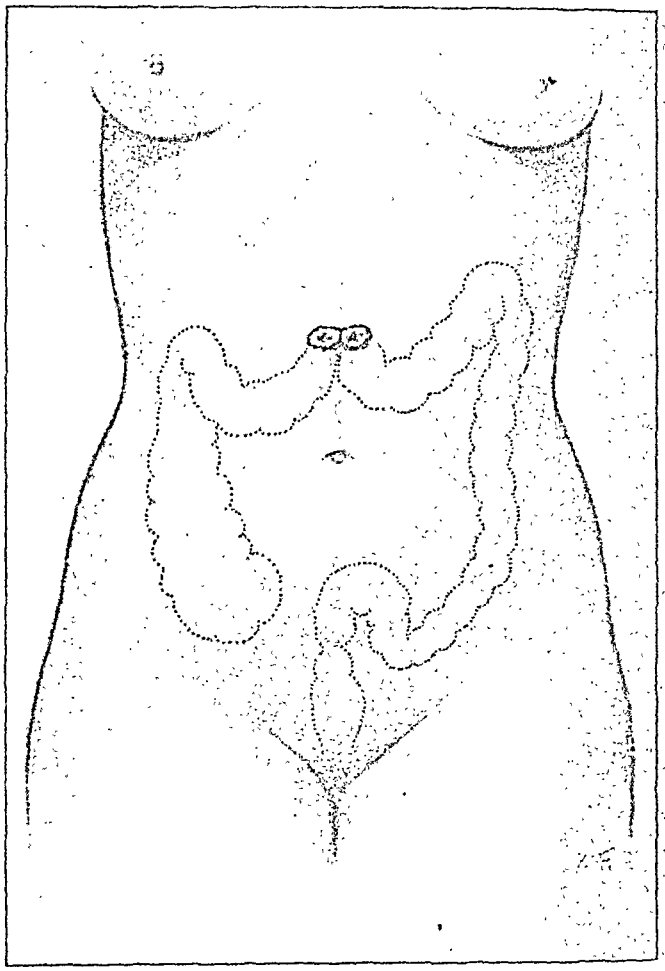
But a large element of truth remains in Treves' valedictory, tho' standardized surgery may be regarded in a different light. In medicine, as in industry, standardization is of great value. In surgery, it tends to a desirable simplification of technic and the scrapping of a multitude of minor variants of fundamental surgical methods, as for example, in inguinal hernia where more than one hundred and sixty named methods for radical cure have been proposed.

As elsewhere, surgical procedures on the colon and rectum are, in the main settled, the resection for neoplasm following well-defined lines and largely governed by the facts of blood supply, lymphatic drainage, the presence or absence of obstruction, infection or abscess-formation. In the surgery of the large bowel, and especially of the left colon, the recognition and treatment of obstruction are of paramount importance. Following the establishment of external or internal drainage—when necessary—the rehabilitation of the patient is taken care of by fluids, glucose, non-residue diet and transfusions. Peritoneal vaccination may be considered advisable and causes little discomfort or danger. At exploration, the decision is made as to the extent of the procedure and the method to be adopted—resection with immediate restoration of the continuity of the gut as in the classic Friedrich operation or the first stage of a clamp-resection of the type of Rankin-Mickulicz. No matter what the method employed, the principles of surgery of the large intestine remain—decompression, mobilization, scrupulous asepsis and resection according to the vascular pattern.

It is true, that surgery of the colon, dominated by the "set operation", offers an acceptable technic for the routine situation. Thus it approaches the professional's ideal: soundly based and practically fool-proof, entirely lacking in excitement, deceptively smooth and effortless.

Adventure is lacking, but, as Stefansson said of adventure in another field, it is the hall-mark of the ignorant, the unprepared and the foolhardy. Yet what might be called "controlled adventure", the pioneering spirit of experimental surgery and the trial and error of the formative days of our surgery—this spirit is to be extolled, this adventurous flexibility, the very stuff and substance of surgical progress.

In illustration of the foregoing, two recent cases are offered.



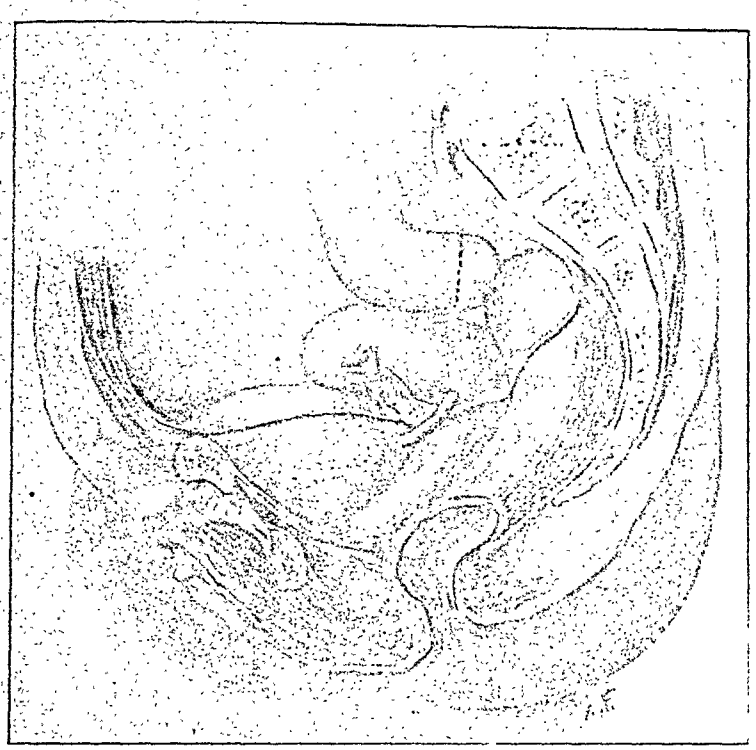
Condition of the patient previous to operation

CASE 1—A white woman, aged 37, referred by Dr. D. A. Lehman, appeared with a "double-barrelled" colostomy, situated in the transverse colon. The pertinent facts were: laparotomy for removal of diseased adnexa seven years previously, followed by increasing constipation necessitating the constant use of laxatives and enemas. Two years previously, she gave herself an enema of very hot oil following which she had severe pelvic pain and long continued diarrhea which resisted medical treatment over a period of six months. A surgeon then performed the colostomy which functioned well, but too often. The constant attention to the colostomy disturbed the fastidious patient and, becoming more and more depressed, she determined on suicide if she could not have the continuity of the colon reëstablished.

Proctoscopic examination showed a complete stricture of the lower sigmoid.

The risk and difficulty of surgery were explained but the patient insisted on operation. Accordingly, under spinal anesthesia, the abdomen was opened and, after considerable

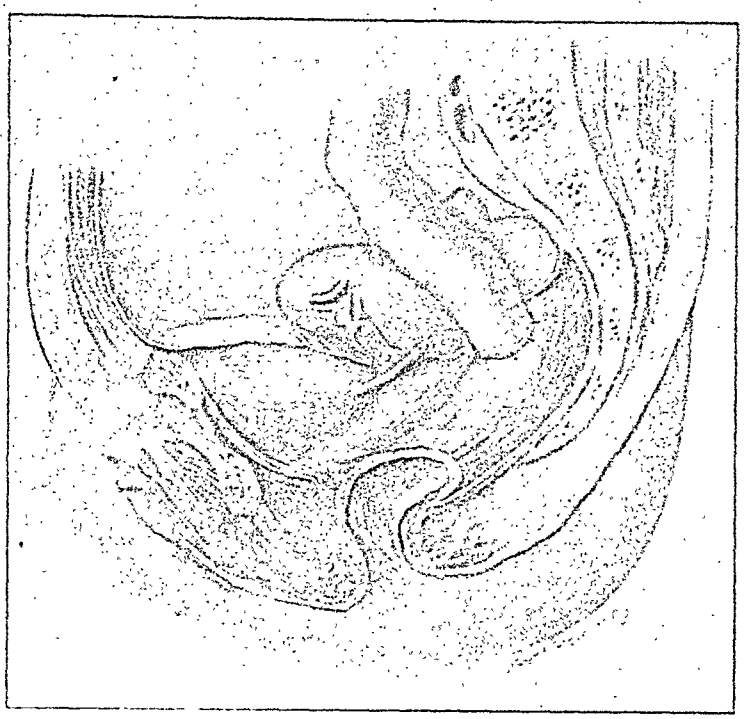
difficulty, the strictured area could be seen, but was so densely fixed that it was necessary to side-track it. The gut was divided in a healthy area proximal to the stricture, the caudad end closed, a rubber tube was passed into the rectum *per anum* and attached to the proximal end of the divided sigmoid which was thus drawn into the rectum through a longitudinal slit at the peritoneal reflection. Anastomosis of the sigmoid to the rectum was then easily carried out. The limbs of the colostomy were then anastomosed, the colostomy and the abdomen closed. Recovery was without incident. The patient has experienced good health since and considers herself cured.



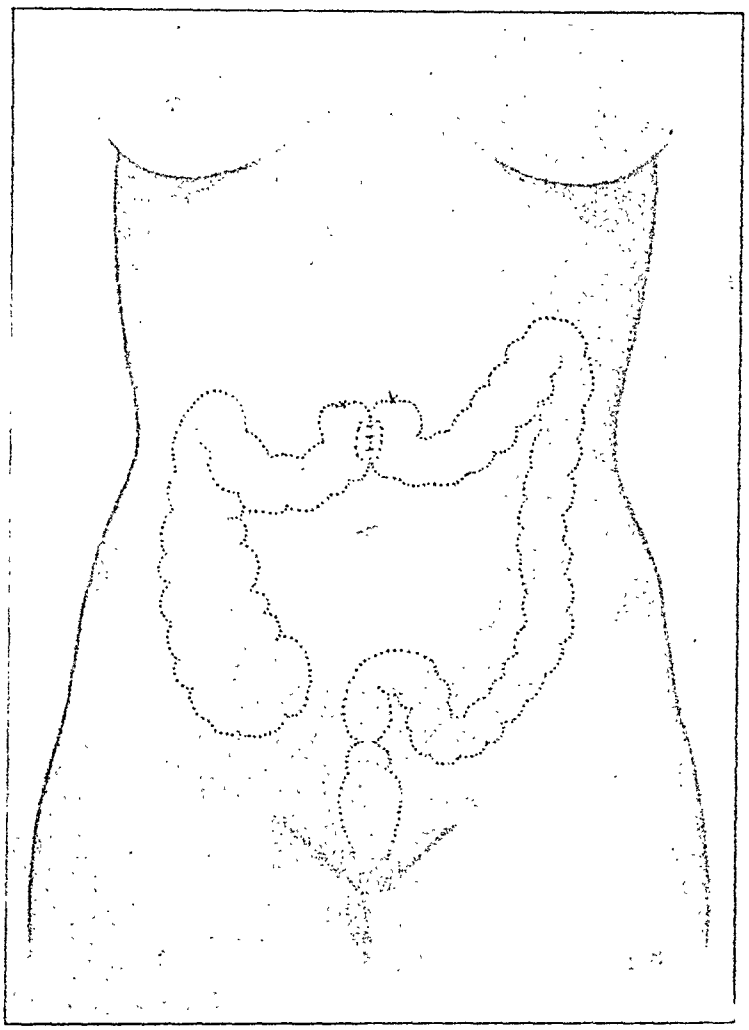
The dotted line shows where bowel was divided above the stricture and the lower end inverted



The tube is fastened in the proximal of the bowel—a slit is made in the rectum—the tube is passed into the rectum and recovered by the assistant at the anus—afterwards the proximal end of the bowel is sutured to the rectum and covered with peritoneum



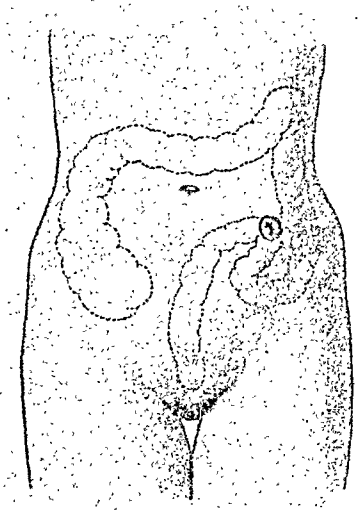
Shows position of the bowel after the final stage of the operation



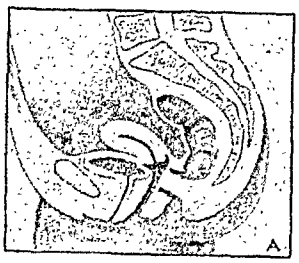
Shows the colostomy after closure, and the new anastomosis to obviate pressure on the closed end of the colostomy

CASE 2—A girl, aged 16, born with an imperforate anus had a colostomy performed when she was one day old. No attempt had been made to explore the site of the *anus*.

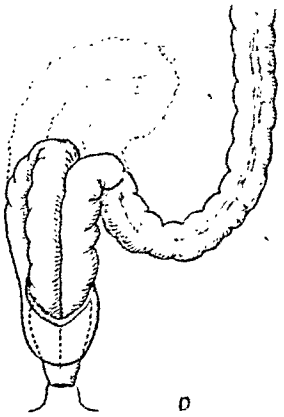
An incision was made posteriorly from the anus, the coccyx was removed and exploration showed the anal canal and the end of the rectum attached to the posterior vaginal wall, with a



Shows position of the colostomy

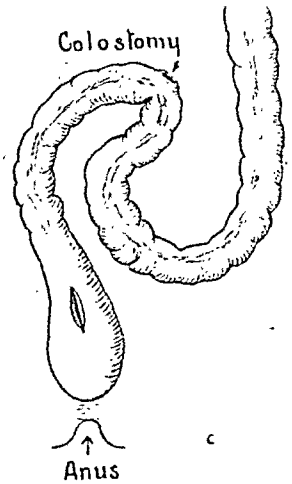


Shows condition at the time of birth



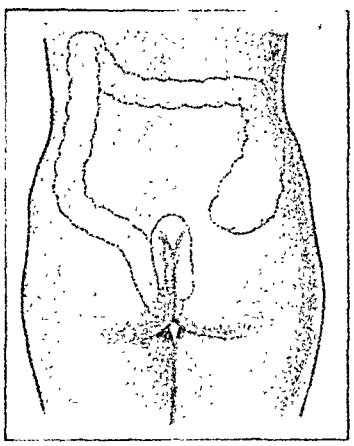
Shows the colostomy separated from the abdominal wall.

well-marked septem intervening. An unsuccessful attempt was made to anastomose the distal end of the bowel to the anal canal. A second operation showed that the distal end of the large gut was strictured above its dense attachment to the vagina. Accordingly, it was decided to clear the hollow of the sacrum and pack it with gauze. Then the colostomy was



Position of the colostomy opening after its attachment to the anus.

completely separated from the abdominal wall and closed. The abdomen was then opened in the midline, the leaves of the pelvic meso-colon were divided, and the gut mobilized. The limbs of the pelvic loop were sutured together and attached to the gauze packing, which on removal from below, brought the loop into the hollow of the sacrum and the colostomy site into the region of the *anus*. Appendicostomy was done through a stab wound and the other abdominal wounds closed. The colostomy stoma was now opened and sutured into the partially denuded anal canal. Convalescence was smooth, the appendicostomy proved superfluous and, in the succeeding year, the girl gained twenty pounds in weight.



Diagrammatic representation of the position of the bowel following the operation

Surgery is not and cannot be stereotyped. With the best available preoperative study, unforeseen conditions will be encountered in the abdomen and the ability to cope with emergency situations will earn large dividends. As has been wisely said, "The best surgeon is the one who brings his brains to the operating room".

MULTIPLE FISSURES OF THE ANUS IN A CASE OF TERTIARY SYPHILIS*

LOUIS A. BUIE, M.D.,
Section on Proctology, The Mayo Clinic
and
WINFIELD L. BUTSCH, M.D.,
Fellow in Surgery, The Mayo Foundation
ROCHESTER, MINNESOTA

LATE syphilitic lesions of the *anus* are so uncommon as to be practically unknown. Recognition of the underlying cause of the rectal complaint in our patient led to the institution of proper treatment.

Harrison Cripps[1] presented a clear description of what he considered to be syphilitic ulcerations of the *anus*: "They are often multiple, and there may be several fissure-like cracks existing between the anal folds, while the folds themselves have a whitish, slightly sodden appearance, the whole part being moistened by a thin, foetid secretion." His description resembles very closely our conception of a mucous patch. He found that these lesions generally appear in from three months to a year after the onset of infection. At the same time, Cripps reported a case in which the condition paralleled that just described; cure was effected by anti-syphilitic treatment carried out for three weeks.

With regard to frequency of occurrence of tertiary syphilis of the *anus*, Sick[10] found only one gumma of the *anus* in 11,826 cases of syphilis. There were thirteen anorectal syphilomas in 4,400 cases of tertiary syphilitic lesions described by Fournier[2]. Anorectal syphiloma, as described by Fournier, is included in the classifications of Hazen[4], Keyes[7], Gant[3], and Yeomans[13]. On the other hand, both Lockhart-Mummery[8] and Tuttle[12] stated that anorectal syphiloma is simply fibrosis of the tissues resulting from previous nonsyphilitic ulceration. Pennington[9] stated his belief that all tertiary lesions of syphilis occurring in this region are confined to the rectum and are in the form of diffuse gummatous infiltration or its end result, stricture. Stokes[11] mentioned only one case of gummatous infiltration of the *anus* and rectum. It must not be forgotten that cracks and fissures or shallow ulcers with irregular borders do occur in the *anus* in cases of heredosyphilis during the first few years of life.

REPORT OF CASE

A white woman, aged fifty, came to this Clinic because of rectal soreness, with "spotting" of blood. This had existed a number of years, which she believed to be ten. She had always considered that the symptoms were caused by hemorrhoids. The pain and bleeding had become much worse during the previous two years, so that each bowel movement had caused her great distress. She had delayed coming to the Clinic for at least a year, because treatments given elsewhere on several occasions had failed completely to afford her relief. The daily use of cathartics and numerous enemas had alleviated, in a measure, the severe discomfort of defecation, which always had been constant, never remittent.

The patient had been married twelve years prior to her visit to the Clinic. Shortly afterward, a profuse vaginal discharge had developed which had been followed by suppuration in Bartholin's gland of one side. Careful questioning failed to reveal any history of the primary or secondary manifestations of syphilis. A serologic test for syphilis never had been made. Her family history was negative for syphilis. She had been in a sanatorium for nine months following an attack of pleurisy which had occurred seventeen years ago. The diagnosis at the time had been pulmonary tuberculosis. Roentgenograms of the lungs made in 1925 and 1932, had given negative results. For the past six years she had had "sharp, stinging, spot pains" in varying parts of her thorax that had lasted less than a minute. These had occurred several times a day, or only once in three or four days.

At examination, October 26, 1933, the pupils were fixed and unequal. A neurologic examination was negative, as was examination of the ocular fundi.

The *anus* was found to be fissured at multiple points: the *rectum and sigmoid appeared normal. The term "fissured"* must not be confused with the term "fissure" as applied to an anal lesion. "Fissure" is used to designate a definite disease-entity, variously called anal fissure, painful ulcer of the *anus*, intractable ulcer of the *anus*, varicose ulcer of the *anus*, and so forth.

Moderate anemia was present. The Kline test was 4+, the Kahn test 4+, the Hinton test positive, and the Kolmer test on the blood 44 V.S.P. There were 42 lymphocytes per cubic millimeter of spinal fluid, and the Nonne test was positive. The protein content of the spinal fluid was 40 mg. per 100 c.c. The colloidal benzoin curve read 012, 103, 333, 310, 000, and the Kolmer test on the spinal fluid was 44444 V.S.P.

A roentgenogram of the lungs was negative for pathology.

A diagnosis of neurosyphilis of the tabetic type was made.

Treatment, consisting of one injection of 0.4 gm. of arsphenamine each week for six weeks, and twelve injections of iodobismitol, given at the rate of two per week, (dosage 1.5 c.c.), was begun one week after admission. Potassium iodide was given concurrently with the arsphenamine and iodobismitol.

Following this course of treatment, the proctoscopic examination was repeated. The original lesions had completely disappeared, leaving reddened areas. In view of the fact that local treatment had not been applied to the *anus*, this response was evidently due to the anti-syphilitic treatment. The patient stated that all soreness and bleeding had disappeared. She still used occasional doses of cascara. Seven weeks after admission the *anus* had entirely healed. The patient had no distress with defecation and had found that cathartics were no longer necessary.

COMMENT

The *constant discomfort* in this case was a significant point in the history. Hemorrhoids or anal fissure is characterized by an irregular course. The amount of inflammation subsides, and partial healing takes place, accompanied by temporary diminution in the severity of symptoms. Then the process is lighted up again, with an exacerbation of all the attendant symptoms.

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TUBERCULOSIS ULCERATION OF THE RECTUM AND SIGMOID AS OBSERVED PROCTOSCOPICALLY*

By

CLEMENT L. MARTIN, M.D.
CHICAGO, ILL.

THE tuberculous lesion appears in the rectum in four forms: the ulcerative, the hyperplastic (fibrous), the miliary, and as an acute diffuse tuberculous enteritis. The ulcerative form is of the greatest clinical importance; the other forms are of infrequent occurrence. Tuberculous ulcers in the intestine are secondary to tuberculosis elsewhere; the lungs are the most common primary focus.

Tuberculous enteritis is a frequent complication of *advanced* pulmonary tuberculosis, as a study of our material shows. At the Chicago Municipal Tuberculosis Hospital 80 per cent of the patients dying of pulmonary tuberculosis exhibit tuberculous enteritis. In one series of patients at the Chicago Municipal Tuberculosis Hospital examined post-mortem, 16.3 per cent had ulcers in the sigmoid and rectum.

Three routes of spread of infection to the colon seem proved: (A) direct, from swallowed tubercle bacilli; (B) by retrograde lymphatic extension; (C) hematogenous. There is adequate evidence for believing that direct infection from swallowed bacilli is a common cause of the ulceration in advanced tuberculosis. Viable, though attenuated, tubercle bacilli reach the ileocecal valve and have been demonstrated in early tuberculous lesions at that site: On the basis of autopsy observations at the Chicago Municipal Tuberculosis Hospital, retrograde lymphatic infection is relatively infrequent. Miliary tuberculosis is rarely seen; it most frequently accompanies general miliary tuberculosis, whose primary origin is in the lung.

SITE OF THE TUBERCULOUS COLON LESIONS

Tuberculous ulceration of the intestine commonly begins in the neighborhood of the ileocecum. The incipient lesion is found in one of three places: on the ileac margin of the ileocecal valve, in the lymphoid tissue of the ileum, or at a point in the cecum at or near where the food currents impinge on the mucosa. From this site the disease extends both upward and downward. It is worthy of note that solitary ulcer of the sigmoid or rectum, described by some writers as a common lesion, did not appear in our series.

THE PROCTOSCOPIC DIAGNOSIS OF TUBERCULOUS ULCERS

In ordinary practice prior to proctoscopic examination, particularly outside of an institution for the tuberculous, the differential diagnosis of a patient exhibiting clinically an ulcerative lesion of the bowel demands the consideration of *amebic* and *bacilliary dysentery, chronic ulcerative colitis, tuberculous enteritis, advanced spastic colitis,* and *neoplasm.*

While multiple ulcers are seen through the proctoscope, parasitic dysentery or chronic ulcerative colitis are usually first to be considered as etiologic agents. Wrongly, in the past, tuberculosis has been of first consideration. Actually, the diagnosis ordinarily lies between amebic ulceration and chronic ulcerative colitis. Rarely, other uncommon forms of lesion have to be differentiated. As seen proctoscopically, tuberculous ulcers are *uncommon in a patient who is able to be up and about.* When real tuberculous lesions are present, the pulmonary disease is nearly always active and far advanced. Even in a patient affected with active pulmonary tuberculosis and simultaneously a non-tuberculous chronic ulcerative colitis (colitis gravis), the differential diagnosis should not be difficult as the proctoscopic appearance of the bowel is quite different in the two diseases.

In cases in which low colon ulceration is due to tuberculosis, the proctoscopic appearance is fairly characteristic. The ulcers are moderately large; they vary from a few millimeters to several centimeters. Their outline is irregular and the edge is usually reddened, thickened and slightly raised and often undermined a distance of a few millimeters; the undercutting may be extensive. Commonly, the ulcer base is covered with a yellow pyogenic membrane which is only slightly adherent and, on its being swabbed away, tuberculous granulation tissue is revealed. The granulations bleed easily but, when dry, appear finely nodular or pebbled. Typical lesions can usually be diagnosed tuberculous from their proctoscopic appearance alone; the atypical forms present difficulty. Not all tuberculous ulcers exhibit all the characteristics just mentioned; healing ulcers, their bases covered with a clean gray membrane, may be interspersed with the active lesions in all stages of progress. The mucosa between the ulcers may be edematous, often reddened and at times dry and atrophic. It is generally normal except for vascular changes. Moderate diffuse redness is common; in some instances areas paler than normal are interspersed with areas redder than normal. This phenomenon gives a diffusely mottled appearance to the bowel wall. The engorged mucosa itself does not bleed when it is swabbed with a cotton-tipped applicator but the fine venules in it may, with a resultant line of oozing marking the vessel's course. In arrangement these vessels form branching (treelike) or parallelogram (diamond-shaped) patterns in the mucosa. While at times such may be visible with any type of acute or subacute colitis, they are fairly constant in tuberculous colitis. They are not visible in all cases.

In the tuberculous lesion, loss of mobility of the bowel is not common. Mucosal ring stricture may occur at the site of a healed or healing ulcer, but tubular stricture is rare. Diffuse contraction of the ampulla and diminution in the size of the rectal valves is rarely seen, unlike the process in chronic ulcerative colitis. In tuberculosis the pathologic sequence is: hyperemia, edema, follicular lymphoid hyperplasia, ulceration, hemorrhage, perforation or healing. The disease progresses from above downward in the bowel.

*Clinical Professor of Proctology, Loyola University, School of Medicine; Attending Proctologist, Mercy Hospital & The Chicago Municipal Tuberculosis Sanitarium.

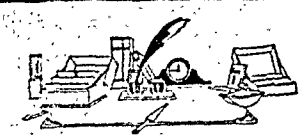
Section VIII.

Editorials

Section IX.

Book Reviews

EDITORIAL



The editorial contributions published in this Journal represent only the opinions of their writers. Such being the case, this Journal is in no way responsible for editorial expressions.

FOREWORD

PRIOR to the issuance of this Journal, there has not been available on the Western Hemisphere a monthly publication exclusively devoted to the printing of authoritative work in the broad fields of the digestive system and of nutrition. Contributions upon such subjects have been scattered through a score of magazines and, usually, without purpose, order or sequence. The interested investigator, clinician and general physician have found that it is a hopeless task adequately to keep familiar with so extensive and widely-dispersed a literature.

Special journals have recorded the work of the experimentor, the internist, the parasitologist, the surgeon, the anatomist, the neuropsychiatrist, the physiologic chemist, the pharmacologist and the dietitian. Few such highly specialized publications are available to the average man; even those with institutional connections experience difficulty in finding time sufficient for as much as the mechanical perusal of a multitude of magazines in a correlated field. When men equipped with special knowledge publish their contributions in journals devoted to miscellaneous but unrelated topics, their theses lose much significance and force, are difficult to locate even shortly after appearance, are limited in respect to completeness and, all too often, their material is *passé* or irrelevant long before it is printed.

The *American Journal of Digestive Diseases and Nutrition* represents an earnest attempt to bring together *in one place* work performed by individuals who, previously, have been compelled to address physicians and experimenters through a great number of independent and, often difficultly secured, publications.

No light burden has been assumed. Incomplete though this Journal may be for some time, experience and coöperation, eventually, will permit approach to the goal set. This Journal is fortunately favored by the support of a distinguished, respected and geographically well distributed Editorial Council. A Council of such character is sufficient proof of there being greater than ordinary interest in the Journal's basic plan. It gives assurance that a serious and persistent effort will be made to establish and maintain this publication in an authoritative position.

It is hoped that the *American Journal of Digestive Diseases and Nutrition* will carry a sincere appeal by its regular publication of judiciously selected contributions from well known clinicians and investigators, by abstracts of the literature which are critical rather than mere statistical compilations, by book-reviews which appraise as well as review, by informative and responsible editorials, by specially prepared summaries dealing accurately and impartially with new or debatable topics, by discussions of therapeutic regimes which have been tested by daily application, by authentic reports of the proceedings of special societies and by illustrative material technically of high order.

It should be unnecessary to state that the spirit and policy of this Journal exclude from its advertising pages all commercial products which are not ethically above question or not made by responsible manufacturers. To business firms which can qualify, the *American Journal of Digestive Diseases and Nutrition* assembles an audience composed of progressive—yet critical and exacting—practitioners and scientists. Gaining favour with a group of such character may prove difficult but, once secured, there should accrue not only the satisfaction which comes from contacts with representative physicians, but also adequate material reward.

F. S.

BOARD OF GASTROENTEROLOGY

Within recent years there has been such an excessive influx of self-styled "specialists" into all the various fields of medicine and surgery, that both the medical profession and the public have become aware of the necessity for some method of regulation of specialism. The ophthalmologists were the first to recognize this necessity, and in 1915, they established the American Board of Ophthalmology, which was incorporated with the object of conducting examinations and issuing certificates of qualification to practice ophthalmology to candidates who applied for such a rating. Since that time over one thousand practitioners have received certificates from this board and it has served as a model for boards subsequently established for other specialties, three of which have been functioning for two years or more, namely, the Board of Otolaryngology, established in 1924; the Board of Obstetrics and Gynecology, established in 1930, and the Board of Dermatology and Syphilology, established in 1932.

Within the past two or three years other agencies stepped into the field of certification of specialists. The New York Academy of Medicine established a plan to grant fellowships in the various specialties represented by sections in the Academy to the existing fellows who could qualify as specialists and to all new fellows, a fellowship in the Academy hereafter being granted only to a qualified specialist. The Medical Society of the State of New Jersey began to work on a plan to certify specialists and tried to get the State to limit the practice of a specialty to those recommended by the Society. State education boards in all parts of the country, universities and medical societies have all been active in this field, and in 1931 the House of Delegates of the American Medical Association commissioned its Council on Medical Education and Hospitals to study the problem, with a view to having this Association assume leadership and bring order out of chaos.

Meanwhile most of the national groups of specialists were organizing boards. The American Gastroenterological Association at its annual meeting in May, 1933, passed a resolution directing that the president should appoint a committee of four to consider the formation of a Board of Gastroenterology and to report at its next meeting. Doctor Burrill B. Crohn, then president, appointed Doctors George Eusterman (Chairman), George Morris Piersol, Harlow Brooks and Walter C. Alvarez to serve on this Committee. Meanwhile there was called a meeting of those interested in the subject of specialty certification and on Sunday, June 11, 1933, the day preceding the American Medical Association meeting, there assembled in Milwaukee representatives of the Council on Medical Education and Hospitals of the American Medical Association, American Association of Medical Colleges, Federation of State Licensure Boards, and National Examining Boards. None of the members of the American Gastroenterological Association Committee being able to

attend this meeting, it was left to Doctor A. F. R. Andresen, of Brooklyn, Chairman of the Section on Gastroenterology and Proctology to represent the Association also. The whole subject of regulation of specialists was discussed in a series of papers by representatives of the national organizations, and in the evening a committee, on which gastroenterology was again represented, met to discuss the organization of an Advisory Council, which should consist of representatives of all the national organizations interested in medical education and of all recognized boards, this Council to coördinate the work of the various existing specialty boards and to establish standards for the organization of new boards. At another meeting in Boston in October, further plans were discussed, and this Advisory Council is to be definitely established at a meeting in Chicago on February 11, 1934.

On the day following the meeting of this group at Milwaukee, a resolution was introduced at the meeting of the House of Delegates of the American Medical Association by Doctor Kopetsky, authorizing the Council on Medical Education and Hospitals of the Association to coöperate in the formation of the Advisory Council of the Specialty Boards, thus giving official recognition to the boards approved by the Council. It is expected that eventually only specialists certified by these boards will be listed in the American Medical Association's Directory.

During the Milwaukee Session, the Section on Gastroenterology and Proctology passed a Resolution empowering its Chairman to appoint two Committees, each consisting of three members, and representing respectively the specialties of gastroenterology and proctology, which committees should coöperate with committees of the national organizations in their respective fields in the formation of National Examining Boards and whose members were to serve on such boards when established. The gastroenterological committee consists of Doctors A. F. R. Andresen (Chairman), Henry L. Bockus and Frank Smithies.

Since last summer the two committees representing the American Gastroenterological Association and the Section have been collaborating in the laying out of plans for the formation of a Board, and at a meeting of the Council of the American Gastroenterological Association on January 21 in Philadelphia, a plan representing the objects and activities of such a Board and the essential requirements of applicants for certification was approved by the Council. This plan must be approved by the Advisory Council of the Specialty Boards before further steps in the organization of the American Board of Gastroenterology can be taken. If approved it will be necessary for the American Gastroenterological Association, at its meeting in May, to place its final stamp of approval on the plan, before the Board can become a reality.

ALBERT F. R. ANDRESEN.
Brooklyn, N. Y.

ENDAMEBIASIS IN THE UNITED STATES

Chicago's experiences with an acute flare-up of chronic or "latent" endamebiasis, nation-wide in distribution, have left certain impressions. Out of the mass of professional and lay statements and opinions some clear-cut facts are evident to practicing physicians.

Present facilities for travel do not admit of any infectious or contagious disease being termed strictly "tropical". No "tropics" are known to infectious agents to whom man may be a host. "Tropics" still is a word in its geographic sense; it is *not*, when one considers disease. Unlimited transportation facilities permit world-wide spread of ailments probably rightly considered "tropical" before the Spanish-American War, or the commercial development of Central America. Infection by *Endameba Histolytica* is one of such ailments.

Even when one estimates its incidence at but five per cent, in the United States, infection by pathogenic endameba is more frequent than are typhoid fever, diphtheria, pneumonia, diabetes, Bright's disease, heart valve disease, cancer of the alimentary tract and, probably, of tuberculosis. Fortunately, not more than one per cent of hosts experience the transformation of their "latent" endamebiasis into its acute or dysentery form. However, it cannot be said that individuals affected with "latent" endamebiasis are in normal health.

With an outstandingly few exceptions, medical faculties, medical students and practitioners of medicine in general still consider endamebiasis as a "rare", "tropic" affection. Despite a score of published articles issued by responsible observers—laboratory workers and clinicians—human protozoiasis finds scant time in medical-school curricula: students receive instruction in learning all sorts of laboratory methods, from isolation, staining and recognition of pathogenic bacteria to performing delicate tests in serology, but, until the Fall of 1933, few, indeed, were the students or their teachers for that matter, who had even the most superficial knowledge of pathogenic protozoa or their effects upon hosts. When the Chicago "epidemic" appeared, it would be liberal to state that in that city there were a dozen individuals capable of achieving exact recognition of *Endameba Histolytica* or other intestinal protozoa. And Chicago was in a position very little different from that existing in other cities of the United States, especially cities north of Mason and Dixon's Line. How could matters be otherwise when clinical protozology had been recognized or taught by but a half dozen medical schools in America? To faculty, graduates or students of medicine, the warnings of impending outbreaks of acute amebiasis meant little: most men either ridiculed the idea or to them the language which had been spoken was foreign. Hence, Chicago's so-called "unpreparedness" should not be held against her: an experience similar to that of Chicago's was—and is—possible in any large community of this country. Undoubtedly, not alone in Chicago but in other northern cities, for years, spasmodic outbreaks of etiologically "obscure dysentery" have been left unstudied by individuals familiar with pathogenic protozoiasis: unquestionably, many instances of acute endamebiasis have been diagnosed and treated as "intestinal tuberculosis", "chronic, ulcerative colitis", "bacillary dysentery" and even colon cancer or its complications.

Chicago's "epidemic" of endamebiasis, grave though it may have been, has served a most useful purpose: it may mean the teaching of clinical protozoiasis in our medical schools by those competent to teach it; it may mean the clinical recognition of both "latent" and "acute" endamebiasis as entities; it should mean more rigid inspection of "truck-farms", of those engaged in such enterprises, of "garden truck" itself with respect to its being clean, of food-handlers (in a wide sense: all those coming into contact with food from farmer to salad-server in hotel dining rooms) and of reducing in numbers the great army of "roughage feeders" who, in the present circumstance, truly are "manure-eaters".

From the conference of experts brought to Chicago, to advise and direct, much of value resulted. Especially important to Chicago and to all large American cities was the evidence furnished that ancient plumbing is a significant factor in the spread of protozoiasis and that much, even "modern" plumbing is not fool-proof to "cross currents", bye-paths, and overflows.

While the experts, in council, emphasized these conditions, their observation was not an original one. When he was Commissioner of Health of Chicago, Dr. Arnold Kegel made an exhaustive investigation of the means by which impurities, chemical bacterial, protozoal, etc., could

do harm in hospitals, hotels and homes. His researches are embodied in the Annual Reports of the Department of Health, Chicago, 1926-30. His recommendations are clearly stated. There is no record that any of Dr. Kegel's recommendations ever received official sanction, though, "in the trade", it is well known that one firm which manufactures an extensive line of plumbing and equipment, expended close to one million dollars in investigation and in the construction of machinery for making "leak proof" sterilizers, toilets, bathtubs, etc. It would seem proper that the efforts of that firm be encouraged and that new ordinances be developed which make it impossible for hotel guests or citizens in their homes to be subjected to the dangers accompanying water contamination. The dangers attendant to the "flood nuisance" in basements of hotels and dwellings likewise received investigation by Dr. Kegel and his associates in the Department of Health, Chicago. It is not of record that, in Chicago, Dr. Kegel's demonstrations and warnings ever were acted upon, although in other cities, they brought vigorous and practical responses.

Perhaps, now that Chicago has been held up before the nation as a city harboring and spreading a dangerous, and, as the lay press styles it, "filth" disease, partisan politics, graft and inefficiency will give way before the indignation of a citizenry which too long has been complaisant or ignorant. However, angry though Chicago's citizens may be at their hygienic betrayal, it is doubtful if any real action will come from those in authority until commercial and business houses see that the "epidemic" of amebic dysentery in Chicago actually is meaning a loss of millions of dollars' worth of business. When this fact has been recognized by commercial interests, then the howl which arises may arouse lethargic public officials to action. It's the loss of dollars, not lives, which hurts.

Hotels, rooming-houses, hospitals, homes in which there is old-fashioned plumbing—in structure and in plan—or where overflow of sewers permits flooding of basements or rooms in which food is stored should be closed by law. They should be kept closed until responsible investigators have certified that food is not stored where sewage backflow can contaminate it with filth. Even if sewage is not a factor in fouling food, investigators, not alone competent technically but who have a keen sense of public justice, must prove that plumbing "leaks", overflows and cross-flowage have been eliminated. It does not suffice for protecting citizens to show that food-handlers are protozoically "clean" if kitchens in which food is prepared and in which foul water has stood a foot deep, are allowed still to prepare and serve meals. If it is shown that a hotel or rooming-house never can be made "infection-proof", then, despite the possibilities of financial loss to owners or lessees, such hostelries must be closed. They should be kept closed, without fear or favor, until they are safe for human habitation. If they cannot be made safe, then they should be denied licence to do business. Human life should be held higher than financial gain. *An example:* six men, on important business, register at and remain constantly in a hostelry for about one week; they eat only food from the kitchens of that hotel; they drink only water supplied there. *Outcome:* within less than two months, five of the six men have died from acute amebic dysentery and its complications. Certainly, permitting such menace as that hotel to exist and *remain* in any community is licencing the right to kill or, if the menace is well known, of giving susceptible individuals—and who is *not* susceptible?—opportunities to commit suicide.

The Chicago outbreak likewise revealed the need for honest thinking, and for those responsible for harboring foci from which pathogenic endamebiasis could arise, to appreciate that Health Officers are *public health safeguards*, not nuisances who can be cajoled into being "good fellows" and signing "O. K." to slips certifying that a menace to life has not existed or has been removed. The Public Health Officers of Chicago had no easy task to carry through and had there not been exhibited grit and persistence by a determined Mayor and an energetic, never-quitting Chief of the Health Department, a lot of sloppy work would have been done. It is to the everlasting credit of the public officials of Chicago that favoritism, political influence and graft never interfered with their work of running down sources of infection and, by the exercise of power conferred by law, of cleaning up places despite efforts to embarrass them. One day, when the present excitement has passed, a dramatic story may be written of the patient and skilled "detective work" carried out before—in spite of clever attempts at deception—the main focus of endamebic infection was discovered. It is a sleuthing yarn as filled with episodes as exciting as are any of those solved by Philo Vance. Trite though is the phrase, nevertheless it is a fact that "Truth *is* stranger than fiction"!

The public press bears a responsibility to its readers. The policy of "hush up" may be one which protects business interests, keeps open stores, permits full advertising columns and brings business offices out of the "red", but a sense of responsibility less selfish should be developed and maintained by the daily press. "Copy", relative to Chicago's flare-up of amebic dysentery, should not be "killed" for out of town—nay, even "home"—editions, or if not "killed" be so printed as to convey the impression that the "Chicago epidemic" is a "false alarm". In the long run, particularly with a successful 1934 session of the "Century of Progress" in view, frankness, meeting the situation squarely, assuming responsibility, telling widely just what has been done and will be done to make Chicago a "safe" city, is the only policy justified by the nature of amebic infection and its possible consequences. Such methods of procedure will do more to restore confidence in Chicago than will "cover up" tactics or the telling of half-truths: "You can't fool all of the people all of the time." If citizens of Chicago or people outside its limits do not get true and complete facts from reading their newspapers, the "grapevine" will convey them. In such circumstances, uncertainty and lack of confidence always will put on matters the worst possible construction. Moreover, the press of cities other than Chicago will do its part—from motives selfish or otherwise—towards keeping people away from "the infested city". A historic maxim long has guided honest, sportsmanlike Americans: "Tell the truth and shame the devil." Truth-telling is the only course capable of restoring confidence. To call Chicago's dilemma "an act of God" is false: poor plumbing, filthy sewers, befouled kitchens and food and the continuance of a folk-infecting business in the face of proved delinquencies, is not to be blamed on God whatever may be one's religion, creed or pliability of conscience!

The Committee of Experts which rendered such signal and unbiased service to Chicago at its recent conference left no recommendation relative to combating the "latent" endamebiasis which, at a conservative estimate, affects five per cent of the total adult population of the United States. This is regretted.

ERADICATION OF AMEBIASIS: "ANTI-AMEBIC WEEKS"

If we, as physicians, particularly as guardians of public health, are to prevent a greater than five per cent incidence of the infection, we must endeavor to exercise such control as will make impossible the appearance of "amebic dysentery", i. e., the "acute" manifestations of chronic, "latent" amebiasis.

The modes of management of the "acute" infection have been established fairly satisfactorily. Through the Bulletin compiled by Dr. Frank Jirka, Commissioner of

Health of Illinois, much information of practical value has been made available to physicians generally, and particularly to Health Officers. Acute amebic dysentery always calls attention to an abdominal upset and since physicians, as well as laymen, now are acquainted with the possibilities of the affection being due to *Endameba Histolytica* proper diagnosis and treatment ought not to be delayed. When symptoms are not characteristic or when fresh stools or cultures from them fail to reveal the protozoa, then, if other ailments can be excluded, anti-amebic therapy should be exhibited "on suspicion". Not rarely, such treatment rapidly relieves signs and symptoms attendant upon what was considered an ailment of obscure etiology.

Therapy in the "latent" or "carrier" stage of endamebiasis is bound to present difficulties; yet it should be instituted if the "acute" manifestations, with dysentery, liver abscess, peritonitis, colon perforation or fibrosis with varying grades of stricture or malformation, are to be avoided.

Manifestly, it is impossible to make accurate stool analyses upon the entire population. Even "one stool" tests which, should a fluid stool be secured, might allow a 30 per cent correct appraisal to be made, physically, could not be performed.

Therefore, it appears to this writer that, since it has been established that infection by *Endameba Histolytica* is widespread in the United States, local or even Federal authorities might accomplish great good—prophylactic as well as therapeutic—by instituting, twice yearly, "anti-amebic weeks". This country has borne patiently so many useless—except to their commercial promoters—"eat-an-apple", "plant-a-tree", "buy-a-car", etc., etc., "weeks", that it's about time that "weeks" be established capable of resulting in real service to our citizens.

During such "weeks"—preferably in Spring or Fall, times at which conditions are most favorable to the development of "acute" endamebiasis—the entire population should be given opportunity of taking anti-amebic remedies. A routine form of therapy, suitable with regard ages of subjects, could be devised and made public by a committee of experts named by the Federal or by State authorities. Potent, anti-amebic medicines are expensive, but if the central or state governments bought and dispensed them on a great scale, they need not cost prohibitive amounts. Physicians should be allowed to dispense these remedies to private patients at the reduced cost; if the patient is unable to pay for the medicines, then the central or the state governments should pay for them. Far more is such government expenditure justified than it is for many projects now calling for vast sums. Untold improvement in the physical welfare of our nation's citizens would follow and the number of instances of amebic dysentery and its complications greatly would be reduced. Just as the regular exhibition of quinine has proved to be of great benefit in malaria-infested sections, so would be the value, through the years, of our entire population's guarding itself against a dread, acute disease by medication given periodically during "anti-amebic weeks".

The procedure is practical. To the writer, no plan other than the one outlined seems possible if we are to make a nation-wide attack upon a life-threatening and life-taking menace.

F. S.

FAMILIAL INCIDENCE OF PEPTIC ULCER

While certain American clinicians have been impressed by the observation that not infrequently more than one member of a given family exhibits gastric or duodenal ulcer, the native literature contains scant reference to the familial incidence of the affection. This is in rather marked contrast to reference to the subject in continental literature.

Riecker considers important Stewart's (England) observations that in view of the fact that the general peptic ulcer incidence in that country is estimated at 10 per cent of the total (adult?) population and that while approximately 5 per cent of peptic ulcers "become cancerous", yet 16.87 per cent of Stewart's cases of gastric cancer arose from what had been considered non-malignant ulcers. It would appear that such observations are weighty with regards the diagnosis and control of both affections.

In Continental Europe, clinicians frequently have stressed the occurrence of peptic ulcer in family groups. Dreshfield noted it in six families; Huber records 30 instances; Czernecki, in mother, son and three daughters; Plant in 22 per cent of 50 cases of ulcer; Spiegel states that in 121 patients, familial incidence could be traced in 26.4 per cent and in the same group the cancer frequency was 14.8 per cent; Menasci observed blood relationship in 26.7 per cent of 71 patients; Zisa in 33.3 per cent.

Riecker reviewed the clinical records of 942 instances of duodenal ulcer at the University of Michigan Hospital with the object, particularly, of determining the significance of familial occurrence. His tables appear to indicate such an etiological (?) factor in 124 of ulcer, cancer of the stomach or both (13 per cent). He calls to mind Spiegel and Bauer's statistics which show that peptic ulcer is four times more common in "ulcer families" than it is in control families and that gastric cancer is six times as prevalent in peptic ulcer than in non-ulcer families.

The Author offers the explanation that results recorded may be considered from two viewpoints (1)—Cancer is inheritable as an organ-predisposition tendency or (2)—that cancer is "engrafted" on the site of ulcer arising in the stomach. Each of these approaches to a clearer conception of the problem may be made of greater value if, in clinical histories, accurate data are tabulated with respect familial incidence of peptic ulcer. However, control series, similarly should be analyzed. For, while the general impression would appear to be that ulcer is a common occurrence in families, so are other "diseases", as gall-stones, rheumatic fever, diabetes and cancer (not involving the stomach?). While it is admitted that the etiology of peptic ulcer is not known (?), the conception of familial occurrence offers opportunity for studying such (predisposing?) factors as environment, food, habits, constitutional type, the psychological "pattern" of patients—all of which have, at times, been advanced as having etiological importance.

Riecker's study carries significant suggestions. His own statistics while not altogether "shot-proof", would appear to have weight in supporting the doctrine in respect familial incidence of peptic ulcer maintained by the late Prof. Aldred Scott Warthin (Annals of Internal Medicine, 1931, IV-*PP* 681-696). However, Riecker's report has so interspersed familial incidence of ulcer with that of cancer, that it fails to leave the impression of facts from which definitely useful interpretations are possible. Certainly, the premise that 942 duodenal ulcers are being studied with respect to their giving information regarding the familial incidence, presumably of duodenal ulcer, soon is deserted for an extremely indefinite discussion dealing with gastric ulcer, gastric cancer, the relationship of each to the other, allergy, etiologic surmisings, etc., with little said about how fared the original enquiry upon duodenal ulcer.

Riecker is not alone in creating such confusion, as anyone will admit after reading the literature which he quotes. Certainly if we are to get anywhere towards estimating with reasonable accuracy how commonly peptic ulcer affects given families, only data which are comparable should be compared. American clinicians, too, must recognize that peptic ulcer as observed in their country is an ailment

The Familial Incidence of Peptic Ulcer, Riecker, Herman J., Annals of Internal Medicine, 1933, Dec. V, pp. 732-737.

far different from that observable in continental clinics—especially those of Germany, Austria and Scandinavia. There the affection is more often gastric, is of a character far more extensively destructive, is more frequently a multiple lesion and usually is accompanied by more serious complications than it is in the United States. Due largely to these differences, continental surgeons have advocated—and perform—almost complete gastrectomy in gastric ulcer management. In Europe, duodenal ulcer still is overshadowed in diagnosis, in knowledge of its occurrence and pathology and in therapy by the more tremendously striking and serious gastric lesion.

The more frequent incidence of lues in Europe and the common practice of using alcoholic drinks from early life may result in circulatory and mucosal changes in the stomach to a degree not observed in America. Hence, peptic ulcer not only appears more frequently there than here but, when once it arises, it is an affection not readily controlled by dietetic and medicinal regimes. The extensive literature upon peptic ulcer—gastric or duodenal—demonstrates so many antagonisms and wholly inreconcilable differences when the studies of various American and European writers are followed, that, long since, clinicians have given up as a hopeless task the attempt to reconcile them. Such attitude would appear warranted. Clearly, different types of a like, but not identical, affection cannot be harmonized for universal statistical, clinical, pathologic or therapeutic acceptance. F. S.

"ENQUIRIES AND REPLIES"

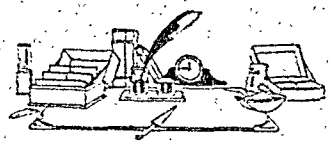
As time goes on, provided there is a demand, the *Journal expects to establish and maintain* a Department titled as above.

To some of our readers, help might be given through a Bureau to which may be submitted problems in technique, diagnosis, therapy and allied subjects.

An endeavor will be made to have answers given by authorities in the fields covered by the enquiries. The personnel of this *Journal's* Editorial Council is assurance that service of a high order will be available. F. S.

If you ordered your Journal and did not get it, think of these possibilities: you may have forgotten to write even your name on the reply card; you may have forgotten to send your card; you may have moved. Please keep the publication office informed at all times of any dissatisfaction.

REVIEWS



This Journal is not responsible for the opinions, decisions or grouping expressed by reviewers of books or pamphlets. For the guidance of readers, an attempt is made to indicate the relative worth of reviewed material by placing "stars"—★ in connection with the reviews. The greater the number of "stars", the more agreeably and importantly does the book or pamphlet impress the reviewer.

★★★★ *"Diseases of the Digestive Tract"* by Arthur L. Bloomfield, MD., pp. 644-739, Musser's *Internal Medicine*, Lea and Fibiger, Philadelphia. 1933.

In conformity with the general plan of the editor, the author of this section has avoided the non-essential and dismissed the unusual and rare with but brief mention. As a result he has presented, within less than 100 pages, a very practical account of diseases and disorders of the digestive tract.

The order of procedure is by organs, from above downwards. Acute tonsillitis is described invariably as a self-limited, specific infection by strept. hemolyticus (beta type of Brown), and this attitude is supported by cultural, and human experimental investigation. Disbelief in the validity of focal, dental infection as a very substantial causal factor in systemic disease comes as a vigorous broadside to an entrenched American assumption to the contrary: but, nevertheless, the eradication of such foci are recommended on their own merits where proper indications exist.

In classifying disorders of the stomach, the common symptoms of dyspepsia, such as fullness, epigastric pain, belching and nausea, are grouped conveniently under the heading of *indigestion*, and this stands in a series with 6 other classes, all organic in nature. In a description of indigestion, it is emphasized that this symptom-group may depend upon lesions either extra- or intra-gastric, or upon nervous influences without organic lesions. Distention of the walls of the gastro-intestinal tube offers the only adequate stimulus whereby pain can be regularly produced. Physicians are more at sea in dealing with this clinical syndrome than in any other department of medicine, since they tend either to minimize all cases of indigestion or to explain all cases on the basis of gall-bladder disease, duodenal ulcer or chronic appendicitis. Perhaps few things are more worth emphasizing.

A good description of the histamine method of gastric analysis with fractional tests is given, along with standard graphs for evaluation of the results, both regarding volume of secretion and degree of acidity. While the author has elsewhere, even more than here, shown the limitations of what may be deduced from gastric analysis, he wisely refrains from discouraging the procedure since, unpleasant as it may be to the patient, many clinicians have come to regard this information in all gastrointestinal cases, as valuable.

Since the diagnosis of *gastritis* depends chiefly on the history of irritating food or drink plus the finding of blood or mucus in the stomach contents, the entity is regarded as hanging by a very thin thread, especially from the pathological standpoint.

The chapter on peptic ulcer emphasizes the constitutional characteristics of the patients and minimizes the etiological role of focal infection. The point is well taken that two duties face the physician: to rid the patient of his symptoms (which is frequently easy) and to promote healing of the ulcer (which is a difficult, often impossible, task). Rest and a bland diet are the factors common to all beneficial regimes, and, mostly, ultra-radical diets and milk-and-powder schedules are to be discouraged. Does the author permit tobacco?

A very conservative chapter on "intestinal neuroses" covers the features of "intestinal indigestion", irritable or spastic colon and mucus colitis, in which the mental and emotional characters of the patient are well portrayed. Psychotherapy must frequently be invoked if any success is to be attained in those patients devoid of organic lesions. Too much dieting, as well as faddism of all kinds, is berated.

The diarrhoeas, both acute and chronic, are well described. Bargen's work on ulcerative colitis is accorded the admiration it deserves, but his microorganism is not regarded as the sole, causal factor. Early operation in suspected instances of acute appendicitis is a safer program than expectant treatment.

Although in cancer of the stomach and the colon all therapeutic endeavor is, in almost all cases, futile, a strong plea for early detection rightly is emphasized.

The Section, as a whole portrays, above all, a practical approach to a very wide and difficult field, and is one of particular value to the student and general practitioner. It breathes a moderate, well-seasoned pessimism in general which, emanating from a keenly scientific and sham-hating mind, is attractive and, frankly, justifiable. Iconoclastic thought is valuable, well-considered conservatism is essential; fearless expression of moderate nihilisms are to be encouraged in the practise of medicine. Nevertheless, progress also is made at times, by the opposite attitude of astigmatic liberalism in treatment. The lovable pragmatism of the general practitioner "who permits what works" has sometimes put us upon the track of valuable clues. To discourage *in toto* all practices which now seem to smack of faddism may be again to place us in the position of needless conservatism which, for many years, lost us the advantage of physiotherapy.

BEAUMONT S. CORNELL.

★★ *"Mystery, Magic and Medicine"*, The Rise of Medicine from Superstition to Science, by Howard W. Haggard, M.D., Associate Professor of Applied Physiology, Yale University. Doubleday, Doran & Company, Inc., Pubs., Garden City, N. Y., December, 1933.

A neatly-bound, attractively-printed, enjoyably-illustrated book, of size conveniently fitting into one's coat-pocket, broadcast *gratis*—(and promiscuously)—by the House of Squibb, potent impressarios in the drug and chemical Guild, and dedicated by the author to the memory of Dr. E. R. Squibb, a pioneer in the advancement of scientific medicine—(and founder of the Squibb concern)—which accounts for practitioners, generally, receiving this book as a surprise in the morning's mail, usually tossed unopened, with a "damn all that advertising junk!" into the capacious office waste-basket.

Trying strenuously to overcome the quite natural handicap of "looking a gift-horse in the mouth", with respect honestly appraising the worth of "Mystery, Magic and Medicine", the reviewer thought that, until he arrived at the reproduction of Sofias', 500 B. C. plaque, showing left-handed Achilles (a bit of a surprise!) doing a very amateurish job of bandaging the "I'll-look-the-other-way-Petrokles" wrenched elbow, (page 30), he would have to "thumbs down" the enterprise. For, to that point, the impression given was that Friend Haggard not alone was reincarnating a considerable lot of material previously printed in his "Devils, Drugs and Doctors", but had browsed in a very inclusive fashion upon the pastures so richly cultivated by Lieutenant Colonel Fielding Garrison in "An Introduction to the History of Medicine"—(has not the author mistitled the Colonel's great book on p. 157?). However, even though, for the following hundred pages (give or take a few) Eli's Associate Professor of Applied Physiology, often, indeed, dips deep his facile pen into Garrison's ink-pot—nay, at times, crowds the eminent Medical

Corps' Officer clear away from it—he redeems himself in satisfactory fashion; in fact, takes away completely whatever *onus* he is bearing in being the sponsor of a "gift-horse".

In exceptionally readable style, often racy, usually accurate, always interesting, Dr. Haggard gives a sharp-etched picture of the halting, if generally forward, course of medical art and science from Galen to Lord Lister. (And not placing out of focus, either, the wise and plodding Dr. Squibb—an achievement wholly admirable both to Haggard and the House of Squibb, who apparently footed the bills for the issuance of the monograph: a no inconsiderable burden in these days of the tortured dollar!).

It's a good job. One would have to make a long search through the literature before he met a hundred, and rather small, pages containing so much history, so many facts, so numerous a personnel (the Author succeeds in giving each adequate elbow-room!), so nice a balance between the essential and the ephemeral and such an entertaining selection of pictures. Further, events, medical, in this country's colonial and pre-civil war eras have been left not unrecorded: a fault all too common with historical writings about our profession. Customarily, while Auenbrugger, the Hunters, Morgagni, Jenner, Semmelweis, Bright, Laennec, Stokes, Basedow, Bernard (giants, it is admitted) loudly have been extolled by many writers, America's early physicians, whose handicaps were prodigious, Shippen, the Junior, Rush, Morgan, McDowell, Nathan Smith, Beaumont, Holmes, Halsted, Crawford Long, Jackson, Warren, have received scant recognition at home and, with the possible exception of Beaumont; even less abroad. Yet let it be recalled, our professional predecessors in the United States pioneered vaccination against small-pox, developed general anaesthesia, recognized and controlled infection consequent upon child-bearing, mastered the ravages of scurvy, rationalized the care of the insane, initiated abdominal surgery and made practical the science of antisepsis, coincident with (often, indeed being original proponents) men of older civilizations, men who long have been placed upon pedestals by their admiring, yet scientifically ignorant and out-of-focus, countrymen. If Dr. Haggard has done nothing else by compiling his little book, he has placed American Medicine in the perspective in which, for more than one hundred twenty-five years, well it has merited.

Coming to relatively modern times, Yale's Physiologist applies himself accurately and diligently enough, but events and individuals so recent as to be within the memory of most of us, of course, lack the awe and glamour of such as arose in years crowded with the vagaries of kings, popes and potentates, the panolpy of war, the deep stirring with religious fervor of the ignorant (if high-placed), the clash of dictators and of the dictated to, and the dramatic pronouncements of such fundamental discoveries as the blood's circulation, the elemental anatomy and functions of the nervous system, vision of the first pathogenic bacteria, the invention of the stethescope, the clinical application of the simple mechanics of percussion, the development of chemistry and the initial ventures into realms opened by major surgery. Without mystery and magic, medicine entered an age of commonplaceness: a time when a man in a given position was expected to perform such acts as his occupation of that position implied. Although, the past half century has seen achievements which dwarf in their originality, scope and importance many of those about which lay and medical historians are accustomed to rave, yet a full century will have to roll around before authors will be able to give them orderly grouping and, in writing of them and the men who made them possible, to throw about their recitals, the fascination and "mystery"—in its prime, sense—which made "great" the days of Galen, Rhazes, Arbuthnot, Sydenham, Hunter, Paré, Parkinson, Basedow, Baillie, Laennec, Bright.

Hence, the end-sections of Dr. Haggard's book to the sophisticated reader seem "stale, flat and unprofitable". Yet, doubtless in them, the layman may find episodes which pop out his eyes with wonder and admiration. Particularly, should non-medically trained folk be interested in the development to practical service of the X-ray, studies in infection and its combating, researches in the chemistry of vitamins, the remarkable fields of endeavor opened by recognition of deficiency diseases (especially pernicious anemia, scurvy, beri-beri) and the success achieved in therapy from special, but near-at-hand-diets, the painstaking efforts to solve the secrets held within the ductless glands and the telling the story of that modern miracle, Banting & Best's gift of insulin to two million diabetics. Possibly, the knowledge that his own Yale has contributed so insignificant a quota to the elucidation of some of the major advances cited, while the rival "Cantabs" have wielded so potent an influence, is responsible for Dr. Haggard's briefness in discussing the marvels of modern medicine. We would do no more than hint this: rather would we consider that the versatile Physiologist would have applied himself just as enthusiastically to reciting the accomplishments of the recent age and time, had he felt that sufficient flavor, as ripening by years brings, could have permeated them.

To those contemplating the study of medicine, to the group already deep in the toils of "getting through" medical colleges, to the vast army of those possessing degrees in medicine (not necessarily those removed from institutions of instruction and the halls of great hospitals, either), to a host of curious laymen and especially to the physician who is starting on what gives promise of being an arduous and profitless consultation-trip and who wishes to slip into pocket or bag, "something to read", the reviewer suggests Dr. Haggard's latest effort. And, it seems but the minimum of courtesy, indeed, when transmitting whatever bouquet is due the Author, to express, appreciation to the House of Squibb for sponsoring a book which not only serves as a tribute to its Founder but carries to thousands of physicians, quite reliably and readably, the story of a great profession, a profession with which Squibb's commercial interests, for three quarters of a century, have been allied closely and, let it be recorded, honorably.

Dr. Haggard's book ends with a "glossary of proper names and medical terms", very informative but a bit of a hodge-podge. Evidently this "glossary" is appended for the benefit of lay readers. If so, it could have been arranged more systematically and intelligently.

There is no formal index. This is to be regretted. Perhaps the Author intends the "glossary" to "pinch-hit" for the omitted index. Such arrangements rarely serve satisfactorily.

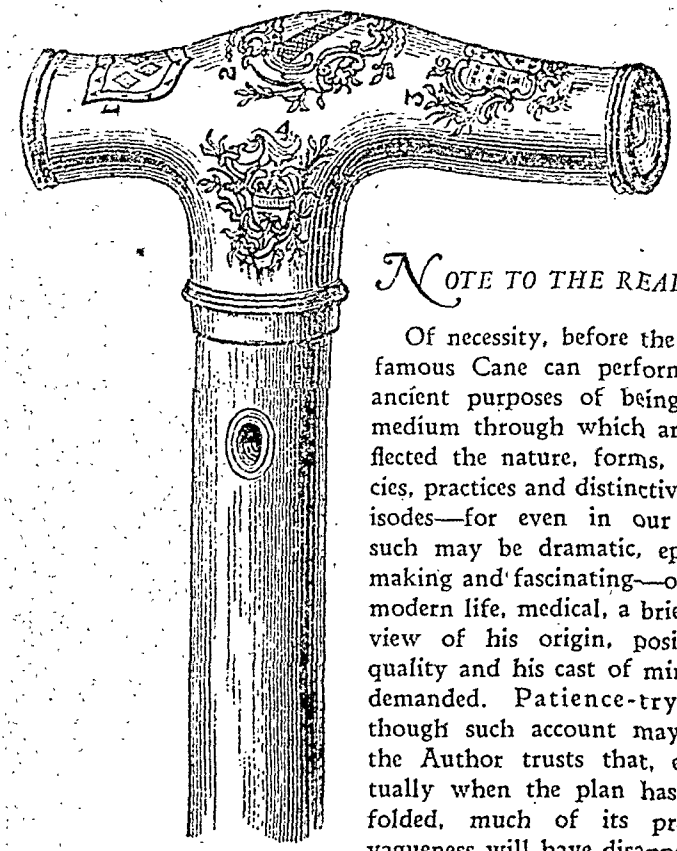
FRANK SMITHIES.

Section X.

After "Hours"

ANONYMOUS

The Gold-Headed Cane



NOTE TO THE READER:

Of necessity, before the now famous Cane can perform his ancient purposes of being the medium through which are reflected the nature, forms, policies, practices and distinctive episodes—for even in our day such may be dramatic, epoch-making and fascinating—of the modern life, medical, a brief review of his origin, position, quality and his cast of mind is demanded. Patience-trying, though such account may be, the Author trusts that, eventually when the plan has unfolded, much of its present vagueness will have disappeared and experiences of an interesting and enjoyable character readily can be forecast.

Certainly, the remarkable chain of circumstances which made it possible for a Gold-Headed Cane, of unusual associations, to leave the famed Library of The Royal College of Physicians, journey to America, there, again, to serve masters of eminence and to participate in events far different from those common to his earlier career, would seem intriguing.

Perhaps an occasional Reader will enjoy a sense of relief in perusing lines not wholly scientific or laden with tales of human discomfort—in which recital the "human" is transformed into a "case", identity lost, a number is affixed, he occupies a "card" and, henceforth, enters the musty realm of "literature", to be tossed from one "bibliography" to another within the covers of existing, nay, even yet unborn, books and magazines. A few, too, there may be who will respect and honor this astonishingly transported Gold-Headed Cane as they were wont to do when former pilgrimages took them to the Library of the New College and when, at the sight of that venerable relic, the roar of London was gone, and in its stead, came delightful visions of an evening session of the scarlet-clad Fellows and the long-stilled voices of Linacre, Sydenham, Hunter, Radcliffe. Some there may be, who will learn to love this mysterious American Gold-Headed Cane for his own virtues and will find pleasure in detailing to the Author episodes in which they themselves occupied a prominence not altogether eclipsed by that of the distinguished traveller from England.

"The active professional career of the original Gold-Headed Cane extended over a period of one hundred thirty years. Born a few months after the flight and abdication of James II, and the accession of William and Mary, in its youth it had the *entree* to the presence of Kings and Queens, and to the mansions of the greatest in the land; in its maturer years, it was carried by its successive owners to the meetings of the learned, to find a resting place, at last, surrounded by the portraits, the literary remains and the spirit of the great physicians of the past, in the College of which they had been distinguished ornaments. There it reposes: in the enjoyment of *otium cum dignitate*." (Peachey, 1923).

A short time before the opening of the New College of Physicians in Pall Mall, East, Mrs. Baillie presented to that learned body the Gold-Headed Cane, which had been successively carried by Drs. Radcliffe, Mead, Askew, Pitcairn and her own lamented husband. (1825).

The Arms of these celebrated Physicians are engraved on the head of the Cane and they form the Vignettes of the five Chapters of the anonymously published "autobiography", titled "The Gold-Headed Cane", which was issued, 1827, by John Murray, at London. It was dedicated to Lady Halford and the edition, so Mr. Murray said, was limited to 1,500 copies. The "Editor" (and author) was William Macmichael, M.D.*

"The Gold-Headed Cane" has passed through five editions (1827, 1828, 1884, 1915 and 1923)—the last,

*Dr. William Macmichael was educated at Christ Church, Oxford, and in 1811, was elected to one of the travelling Fellowships, from that University, which were founded by the generous Dr. Radcliffe—first owner of the Gold-Headed Cane. In compliance with the conditions of the Fellowship, Dr. Macmichael passed several years in foreign travel, mostly in Greece, Turkey, Palestine and Russia. In 1819, he sent to the Press an interesting account of a journey which he had made from Moscow to Constantinople in 1817-18. On settling in London, Dr. Macmichael attracted the notice and soon secured the patronage of Sir Henry Halford (later a President of The College of Physicians succeeding Dr. Matthew Baillie), who, when at the height of his success, and when his duties at Court were the most onerous, found it necessary to have in reserve some physician, on whom he could implicitly rely, to act as his representative; his choice fell on Dr. Macmichael, who through Sir Henry's influence, was appointed, in rapid succession, Physician Extraordinary to the King, Librarian to the King, in place of the very eminent Physician, Dr. Gooch, recently deceased, and finally, in 1831, six years after the death of the last owner of the Gold-Headed Cane, Dr. Baillie, Physician in Ordinary to the King.

Dr. Macmichael took a lively interest in all that concerned the College of Physicians and cooperated more actively than any other of the Fellows with the President (then, Sir Henry Halford, his patron), in the exertions which were necessary to give *éclat* and insure success to the evening meetings. It was during the period of 1824-1829, when Dr. Macmichael filled the Office of Registrar of the College, that, anonymously, he compiled from the records of the Library and from his own recollections, the material which purported to be the Autobiography of The Gold-Headed Cane (1827). The scholarly character of these notes, the unique nature of his observations upon historic occasions and celebrated personages, not necessarily of his "own" profession, his comments upon medical practice, its foibles and the scientific advancements of nearly a century and a half of London's development, brought Dr. Macmichael's thesis instantly to popularity. John Murray's issue of 1,500 copies was so eagerly sought that within less than a year, labour began upon a second 1,000 copies (1828).

Dr. Macmichael was fond of society and was well qualified alike to enjoy and to embellish it. He had travelled long and seen many cities and had observed the manners of many men. In addition, he possessed a large stock of general information. He was fertile in various and amusing anecdote and was wont to mix with ease and grace in lively and entertaining discourse, without making his own share in it unduly prominent; his cheerfulness, equanimity of temper and his kindness of heart endeared him to a large circle of devoted friends.

An attack of paralysis, about two years before death, compelled Dr. Macmichael to withdraw from active life. He retired from Half-Moon Street to Maida Villa, where he died in 1839, aged fifty-five. (Munk, 3rd Edition "The Gold-Headed Cane", 1884).

edited by George C. Peachey, London, is a most comprehensive and complete book, with original notes and beautiful illustrations. The 1884 edition of William Munk, M.D., F.S.A., Fellow and late Senior Censor of The Royal College of Physicians, however, should not be neglected by the curious. This edition carries the autobiographical musings of The Cane through the College Presidencies of such unique and outstanding physicians as Sir Henry Halford (Dr. Henry Vaughan), Dr. John Aryton Paris, eminent scientist and philosopher; Dr. Thomas Mayo, metaphysician, classicist and practical psychiatrist, to the year 1871.

Mayo was the last of a line of strong, individualistic and outstandingly successful London physicians who were honoured by election to the Presidency of the Royal College. Each of these men had, for a period of their careers, dominated London. But London itself was changing rapidly: in size and population it became too huge for any one physician to attend its ills. With this expansion, a score of doctors shared what once had been almost the "eminent domain" of him upon whom Fortune had smiled. After 1871, never again was the city to witness so long and continuous a line of men to whom culture and learning had come as a birthright and to which qualities, scientific attainments, professional skill and participation in the dramatic events of the age, had contributed to their becoming giants, not alone in their profession, but in the history of the times.

FURTHER EXPERIENCES OF

"THE GOLD-HEADED CANE"

ANONYMOUS

Some fifty years of confinement in the corner-closet of the Library of the New College of Physicians gave me ample time for reflection. During the early years of this enforced retirement from active participation in the affairs of the great and the near-great—professional and lay—I experienced the restlessness and discontent which would be expected of one who, even if only passively, had played a part in so many dramatic scenes and on so numerous important occasions. Surely the reader can realize that such idleness was a soul-trying experience and so it proved to be, until I developed a certain philosophic calmness and detachment of mind wherein I could reconsider in perspective the peculiar characteristics of my several masters and the interplay of events and forces which had so influenced affairs, medical, during the one hundred thirty-seven years of what I (not without some degree of personal pride) considered "my practice". Gradually, this solitude of older age and its opportunities for retrospection became a routine which I prized and cherished: a situation which, when I had observed it in elderly men during my young and very active years, I was unable to understand—indeed, formerly the inactivity of the "ancients" was to me a source of wonder, if not of pity mixed with a bit of scorn. At that early period I failed to realize that the late years of life may be pleasantly contemplative and that those men, who through physical incapacitation or on account of the weariness consequent upon the strenuous efforts of their careers, verily are entitled to enjoy hours of peaceful rumination upon events which have led them to high place or to particular distinction.

Thus, gradually, my days became so thoroughly occupied with living again the stirring episodes through which I accompanied my late masters, the eminent Drs. Radcliffe, Mead, Askew, Pitcairn and Matthew Baillie, that what previously I had considered the gloom of my present abode, became an atmosphere richly peopled with those distinguished personages with whom I had been associated. Indeed, so pleasant became the hours of solitude and reminiscence, that the affairs of the Library intruded nowise upon my contentment. Naturally, noises and voices in the hall adjacent to my cozy corner-closet, not infrequently reached me, but only at rare intervals was I aware of their significance. Such occasions arose when, on special meetings of The College, a favoured few were led to my abode and with evident pride—in which, so illustrious had been my career, I, too, shared: at these times, my satisfaction must have been evident by the increased lustre assumed by my famous golden head and the brilliant polish of my hard-wood staff—the Custodian displayed me to groups of scarlet-clad Fellows. Alas, I regretted often, that the courtesy and the proper demeanor which my years of contact with the noblest and proudest in the land, prevented my correcting or supplementing the accounts of my history which the obliging, though frequently not overly erudite, Custodian repeated. As years passed, not alone did, what to me had been experiences of the greatest moment and of the happiest flavour, escape recognition by succeeding Custodians but, sad to relate, the very language in which important episodes in my career were described degenerated from the stately and elegant conversation of my active days to inconsequential loquaciousness. Indeed, at times, I became somewhat suspicious that, interested though the scarlet-robed Fellows might be in my former masters and our historic associations, certain Custodians, overly impressed with the glamour of their official rating, began to regard presenting me to their betters as a wearisome task. Perhaps this attitude was responsible for the circumstance that as the years passed, less frequently was my closet-door opened and, hence, but rarely did I come forth into the dimmed light of the now much-changed College Library.

These far-separated releases from my closet impressed upon me, however, that not alone had there been a change in the quality of Custodians from the year of 1825, but the entire physical aspect of the Library constantly was metamorphosing. When, with tears of genuine affection, the charming Lady of my last Master, Dr. Baillie, had entrusted my future to the Governors of the College of Physicians, the Library Hall—spacious and splendid though it were—in truth was the ideal meeting place of scholarly men: men who loved to handle the huge, shredded, calf-bound tomes, flutter through the pages of musty manuscripts, writ by pens long at rest, and linger —and I must confess, often doze—at ease before the smoke-dimmed portraits which in massive frames adorned the walls of that noble hall.

The fleeting years brought strange differences. Not alone did the Library become peopled with a more numerous group of physicians—many, if I could be relied upon to estimate from my career among the *elite* of the profession, who exhibited beyond question intellectual and scholarly qualities—a group less leisurely and meditative, rarely gathering before a sculptured head or about an ancient scroll in erudite discussion, or speaking the Latin tongue with ease and preciseness. Haste and even discourtesy seemed more and more to characterize the visitors to the Library: oft was I shocked and pained to note with what irreverence certain prized possessions of the Institution were handled: folios and manuscripts which bore the imprint of famous houses and recorded observations which in my day had thundered through the scientific world and

provoked flame-hot discussion not alone among the disciples of Aesculapius but among enlightened laymen even up to the Throne itself. But seldom did a visitor appear to whom the significance of our epoch-making books was evident. Such an one was a welcome sight to me on the rare occasions when it was possible for me to see him; one old servitor whose wrinkled skin matched the parchment of the ancient folios and upon whose spare, bent frame hung coat and pantaloons shiny with years and loose as molly-bags, grew bright-eyed to such a visitor, became nigh three inches taller in stature and changed his scraping steps almost actually to walking, when opportunity arose to fetch and display such treasure as our *De contagionibus*, the masterpiece of the celebrated Fracastoro. Quiet-voiced and modest, time-giving and gentle—and, I must confess, all too often most thriftily-clad—were these whom quickly we came to recognize as scholars of distinction. So few they were, however, that in the darkness of my musty closet, I wondered if it were wise even to maintain our magnificent College Library at such vast expense and again, how came it that these few true scholars fared so poorly in the distribution of worldly goods. A sad contrast they were to those red-faced, harsh-voiced, bustling colleagues, garbed by London's most expensive tailors, shining with watch-chains and rings of heaviest gold and always accompanied by some meek and servile person whose office appeared to be to read, abstract and compile the knowledge which, later, of my very self, I have heard declaimed in far-reaching voice, at assemblages of the College, by the arrogant gold-gatherer. And, need I add, that on such occasions, the hours of labour devoted by the essayist's self-effacing secretary never were spoken of! To the assemblage of modern Fellows of the College, such pirating of the studiousness and of the brain of another appeared to excite no comment, if I may except the occasional side glances and whispered remarks of several of those whom, upon close scrutiny, I recognized beneath their scarlet robes as men who, in the Library, we listed as our small group of scholarly men.

Something akin to heart-sickness affected me at such experiences and on more than one occasion, I found myself wishing that the good Widow Baillie had restrained her impulse to perpetuate the memory of her distinguished husband, Dr. Matthew, by bestowing me into the care of the College—there to remain, at ease, to be sure, but dulled by confinement and inactivity—and had allowed me to pass on to other worlds in the firm hand-clasp of my last master when he was borne in solemn state and reverent silence to his grave.

However difficult it may be to convince to the contrary the peruser of these random autobiographical notes, I must confess that my more than a half-century of seclusion in the dusty corner-closet of Library Hall drifted by so evenly and peacefully that the particular stamp of any individual year left no great impress upon my recollection. In truth, so few were the adventures experienced that such as came to me stand out in sharp etched pattern.

It was an abominably hot morning in the month of August of the year 1875, when the quiet and gentle rhythm of my life suffered one of its most memorable—and, for a brief interval, actually soul-racking—interruptions. So humid had been the atmosphere of the previous day that, before abandoning his labours, I observed that my Custodian neglected locking the door of my abode, nay, actually departed the Library leaving it ajar a fraction of an inch. Grateful as I was for this somewhat unexpected kindness which most certainly assured me that the hours of night would not be so close and breathless as I had anticipated, none the less, I could not but help pondering over so unprecedented an action. Never since I had been placed in my cabinet had some worthy failed scrupulously to visit me at the day's end, to make certain of my presence—perhaps, with kindly intent, alter the position in which I had stood stiffly throughout the long hours—and, finally, close carefully the door and make fast the lock. Little imagination is requisite to make definite the realization that, to me, the many thousands of times at which my door became locked emphasized the close of day and that, for a considerable period, my reveries no longer would be interrupted by my exhibition to the occasional curious or the actually serious-minded visitor. Strange though was the feeling of being left for the night in my unlocked corner-closet, with what dangers attendant thereon left to speculation, yet I could but feel most kindly to my Custodian for his thoughtfulness in so leaving me that it was possible freely to breathe deeply the sweet evening air: for in truth, he appeared a somewhat surly fellow, one in whom such act of consideration might not be expected. Therefore, it was with satisfaction that I passed towards the hour of slumber, deeply regretting the hastily-formed impression that my Custodian was lacking bowels of compassion and reflecting how oft it may be in life that we hastily condemn those to whom nature has failed to be choice of a pleasing visage or gentle manner. Before lapsing into sleep, my resolve had been that never again would I permit the external appearance or the unanalyzed actions of an individual at once to condemn him to my disfavour.

With this pardonable interruption and justification of the seeming neglect or perhaps the studious thoughtfulness of my Custodian, let me once more return to the exciting events of the before-mentioned stifling-hot morning of August in the year 1875. Then it was that, unwarned, I was aroused from my somewhat restless sleep by the sudden opening of my abode. Such intrusion upon my privacy seemed most reprehensible and inconsiderate when, as the door swung wide, I observed that the hour was of uncommon earliness. These unusual events compelled me but to sense happenings of the greatest import. For, as my eyes grew wide, I observed that the day was so young that the sun still sent his nearly level beams through the lofty windows of our Library, casting over the floors and cases most curious and intricate shadow-patterns. Such being the hour, it became, at once, evident that no person of quality or erudition could be abroad to interest himself in my concerns. For, indeed, in that historic age, physicians, scientists and the distinguished of the laity—people of the class with whom it was customary for me to associate—rose but rarely before the hour of noon, albeit, in the case of physicians, emergencies of much portent should draw them from their luxurious couches. Although not all of my late Masters were of the fibre of Dr. Radcliffe, who esteemed it of the greatest pleasure to be one of a convivial and, as history has shown, noted company which gathered early and remained, often in truth, distressingly late in the Old Room at the Mitre Tavern in Fleet Street, yet, even the scholarly Dr. Mead and the almost oriental-minded and circumstanced Askew were wont to sit in learned discourse and argumentation with men of similar qualities until the small hours of morning. It was, and I doubt not still is, the convenience of those placed high in life, to find that the day's greatest joys begin when quiet descends upon the earth and Luna's silvery beams conduce either to jovial companionship or the communion of kindred spirits in intellectual exercises.

Consequently, when my closet-door was opened so near to dawn upon that particular August morning and the creaking of its hinges resounded painfully and loudly throughout the solemn silence of the Library, it betokened an occasion not connected with the affairs of the College or its Fellows, so few of whom could yet be free from Morpheus' arms and surely not attendant at the Library.

For no long time was I left to my own surmises: the harsh hand of a dingy, smock-garbed person seized upon me roughly. So roughly and suddenly roused from rest, at first I must confess, though much as my life had accustomed me to the facing of strange situations, I quivered (I trust not noticeably so) throughout my very length: but not from fear I would have it understood. Oft indeed, in my younger days, in emergency, I had served even so hazardous a purpose as a foil to the keen-edged rapier of some of England's (aye, and those of France!) most skilled and vicious fencers. It came quickly to my yet incompletely functioning senses, that a dastardly, malicious or cupiditous theft was about to be perpetrated. Whether for the sake of the worldly value of my well-known and famous head of bullion-fine gold or to satisfy the crazed and selfish ambition or desire of an unbalanced mind, the College was about to lose one of its rarest and most cherished possessions!

Needless it was to sound an alarm: the Library was solitary as a moon-dark grave-yard. Not for hours would it be peopled with its throng of ancient servitors or Custodians: of those who laboriously compiled our catalogues, copied excerpts from multi-languaged tomes, set straight the rows of massive volumes, worked with slow and painstaking effort (oft in pride and lovable adoration) at bindings, pricelessly fine and individual, or laid, snugly under glass, the newly-bought and vividly-coloured maps and manuscripts. From our few, but stout, Custodians and bushel-men, I could expect no help: later than ever did they now appear, for within recent years, a sort of lower-class guild or union had been devised whereby, no longer could an honest fellow work through lengthy hours or with a natural, sterling vigor, but come he must and go he must and labour only this way and that, were he to retain his wage and place with those fellows of his kind. Although, to me, the present situation appeared so pregnant with possibilities, catastrophic both with respect to myself and, doubtless, (and this I say not in egotistic smugness), even more so to the College and its Fellows and Noble Patrons, through my mind it passed quickly and impressively, how grateful and reassuring, at the particular moment, would be the presence of those stout lads who in former days were wont to commence their tasks by the light of massive, waxen dips!

Alas, my fate seemed sealed. Too soon, indeed, I should experience the exquisite anguish consequent upon the violent wrenching of my celebrated and gleaming head from its well-tried and universally honoured staff. The mighty heat and the acrid fumes of the demoniacal smelter's cauldron seemed, already, to torture and to suffocate me. Shapeless in solid mass, I could envision my golden head, and in that formless lump of metal, lost were the proud arms of Radcliffe, Mead, Askew, Pitcairn and Baillie which, so recently, in delicate tracery, had added distinction and merit to my already-illustrious and serviceable *caput*. Modest and retiring though I am by nature and from long association with the noble, elegant and learned, in the present circumstances, I could but realize and regret that with the demolition which to me appeared so imminent, there would pass from the realms of science, culture, art, nay, even history, something wholly irreplaceable, just as, in truth, had it so occurred when each of my five late, distinguished Masters had departed this earth.

Then, difficult though I find it to explain to you, the *confidant* of these memoirs, then it was there came a strange and sudden calm: a peaceful, philosophic resignation which lessened the tightness of my thorax, gave respite to my racing pulses and eased the throbbing and the calor of my temples. Despair and the choking fear which had clutched my throat, starved my lungs and surely must have dyed my face with an apoplexy-threatening cyanosis, were no longer mine. Instead, I experienced the advent of a comforting quietude of soul in which I rejoiced immensely. For it seemed a satisfaction close akin to that which oft I had envied when I learned of how some legendary hero or a noble warrior of our own turbulent times, leading a mad but gallant band, had perished while gaily scenting a flower, or ignored the fatal blow, to set astride the fastest horse a boyish page that he alone might escape the universal extinction! Such degree of pious happiness, as I now possessed, must have been the strength of martyrs old, who, when the unjust axe of arrogance and hate, high were poised, enjoyed the hasting seconds' interval between this life and future mysteries, with treasured phrase of Plato and of Aristotle! Such joy at dissolution's threshold, could but explain how knightly men crossed it, smiling, as to them an ancient ballad came, melodious with love's sweet nothings!

How greatly more in tune with my gentle birth and orderly years of noble association was this changed attitude! I could but condemn myself for what previously seemed a varlet-like demoralization in the presence of impending annihilation. Of course, some small degree of grace might be assumed since when, roughly, I had been snatched from my snug abode, my senses, still, were numbed by drowsiness and a mind, commonly alert and not untried for resoluteness and with some reputation for courage, not yet fully comprehended the emergency's details. Be as it may, the present consolation suffused my frontal lobes—the centre in which, the late distinguished Dr. Thomas Mayo had proved conclusively at a memorable session of the College, lie all the attributes of reason, courage and control.

To struggle with my lowly-born and knavish captor, in truth, was not for one of my quality: for when, did one of station high as mine engage in rowdy scufflings? Cuffs to his ears or well-deserved whacks across his smock-clad shoulders—a punishment earned, though in administering it my dignity seriously would have been imperiled —were out of question. So firmly was my Golden Head gripped by the calloused hand, that, deep may have been my anger and strong the impulse and desire, defence or resistance was impossible.

With scant consideration, I was taken from my abode and, with steps far more leisurely than would be expected in one whose purpose were to steal from out the Library so famed a relic as years and associations had combined to make me, this early morning kidnaper crossed the wide expanse of the stilled and lofty Hall.

(To Be Continued)

SOCIETIES, PROGRAMS AND PROCEEDINGS

ANNUAL SESSION
of the
AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION

PRESIDENT
DR. JOHN BRYANT, *Boston*
FIRST VICE-PRESIDENT
DR. B. B. VINCENT LYON, *Philadelphia*
SECOND VICE-PRESIDENT
DR. NOBLE WILEY JONES, *Portland, Ore.*
TREASURER
DR. A. H. AARON, *Buffalo*
RECORDER
DR. SARA M. JORDON, *Boston*

SECRETARY
DR. RUSSELL S. BOLES
Rittenhouse-Plaza
Philadelphia

MEMBERS OF THE COUNCIL
DR. LUDWIG KAST, *New York*
DR. CLEMENT R. JONES, *Pittsburgh*
DR. BURRILL B. CROHN, *New York*

COMMITTEE ON ADMISSIONS AND ETHICS
DR. GEORGE B. EUSTERMAN, *Rochester, Minn.*
DR. JOHN L. KANTOR, *New York*
DR. FRANK D. GORHAM, *St. Louis*

PROGRAM

MONDAY, APRIL 30, 1934

MORNING SESSION, 9:00 A. M.
Hotel Traymore, Atlantic City

PRESIDENTIAL ADDRESS
DR. JOHN BRYANT, Boston, Mass.

In Memoriam

DR. THOMAS W. GRAYSON *by* DR. CLEMENT R. JONES
DR. F. H. BAETJER *by* DR. THOMAS R. BROWN

1. "The Humoral Factor Producing Gastric Inhibition Following Carbohydrate Ingestion."
 Dr. J. P. Quigley, Cleveland, Ohio.
2. "Inflammatory Lesions of the Small Intestines."
 Dr. Phil Brown, Rochester, Minn.
3. "The Relationship of the Gastro-Intestinal Tract and Diet to the Deficiency Diseases."
 Dr. Maurice B. Strauss (by invitation), Boston, Mass.
4. "Cincophen Poisoning."
 Dr. Leon Bloch, Chicago, Ill.
5. "Gastro-Intestinal Factors as a Part of the Metabolic Causation of Arthritis."
 Dr. Ralph Pemberton (by invitation), Philadelphia, Pa.

12:00 P. M.

THE ALVAREZ LECTURE
Founded in 1929 by Dr. Frank Smithies
Lecturer to Be Announced Later

Adjournment for Luncheon, 1:00 P. M. to 2:00 P. M.

2:00 P. M.

6. "Pancreatitis—Diagnosis and Treatment."
 Dr. V. C. Rowland, Cleveland, Ohio.
7. "Newer Physiology of the Pancreas."
 Dr. Arthur C. Clasen, Kansas City, Mo.
8. "Diabetes Mellitus, Its Physiological Essence and Rational Treatment."
 Dr. W. M. Boldyreff, Battle Creek, Mich.
9. "Gastric and Pancreatic Enzymes."
 A Report of the Enzyme Committee by
 Dr. A. H. Aaron (Chairman), Buffalo, N. Y.
 Dr. H. L. Bockus, Philadelphia, Pa.
 Dr. A. C. Ivy, Chicago, Ill.
10. "The Bacteriology and Certain Clinical Features of Chronic Ulcerative Colitis."
 Dr. T. T. Mackie (by invitation), The Cornell Clinic, New York, N. Y.
11. "An Experimental Study of the Lower End of the Esophagus."
 Dr. M. Feldman, Baltimore, Md., and
 Dr. T. H. Morrison, Baltimore, Md.

Executive Session at 5:00 P. M.

ANNUAL DINNER, 7:30 P. M.
Hotel Traymore, Atlantic City

TUESDAY, MAY 1, 1934

MORNING SESSION, 9:00 A. M.

12. "Diseases of the Portal Vein."
 Dr. James F. Weir, Rochester, Minn.
13. "The Importance of the History in Gall Bladder Disease."
 Dr. Martin E. Rehfuss, Philadelphia, Pa.
14. "Studies on Alteration of Function in Biliary Tract Disease."
 Dr. I. S. Ravdin (by invitation), Professor of Research Surgery, University of Pennsylvania.
15. "Lowering the Mortality from Appendicitis."
 Dr. J. Russell Verbrycke, Jr., Washington, D. C.
16. "The Importance of Inheritance in Disease to the Gastro-Enterologist."
 Dr. Madge Thurlow Macklin (by invitation), London, Canada.
17. "The Epidemiology, Diagnosis and Treatment of Amoebiasis."
 Dr. Frank Smithies, Chicago, Ill.

Adjournment for Luncheon, 12:00 M. to 1:00 P. M.

1:00 P. M.

SYMPOSIUM ON PEPTIC ULCER

18. "The Significance of Alkalosis in Treatment of Peptic Ulcer."
Dr. Sara M. Jordan, Boston, Mass.

19. "Aluminum Hydroxide in the Treatment of Peptic Ulcer."
Dr. Victor C. Myers, Cleveland, Ohio.

20. "The Niche as a Criterion of Healing in Peptic Ulcer."
Dr. Jacob Buckstein (by invitation), New York, N. Y.

21. "The Treatment of Peptic Ulcer Based on 1,435 Cases."
Dr. Edward S. Emery, Jr., Boston, Mass.

22. "A Rationale for the Treatment of Peptic Ulcer."
Dr. A. B. Rivers, Rochester, Minn.

23. "The Incidence of Gastro-Jejunal Ulcer following Gastro-Enterostomy in 143 Cases."
Dr. J. W. Hinton, New York, N. Y.

The following Papers will be read by title:

"Studies in Nocturnal Secretion."
Dr. Asher Winkelstein, New York, N. Y.

"Chronic Cardiospasm—Its Diagnosis and Treatment."
Dr. E. B. Freeman, Baltimore, Md.

"A Report of a Case of Pernicious Anemia with Normal Gastric Juice."
Dr. A. L. Levin, New Orleans, La.

EIGHTEENTH ANNUAL CLINICAL SESSION OF THE AMERICAN COLLEGE OF PHYSICIANS

The Eighteenth Annual Clinical Session of the American College of Physicians will be held at the Palmer House, Chicago, Illinois, during the week of April 16, 1934. Dr. James B. Herrick, Chicago, is General Chairman in charge of the preparation of the program of clinics and local arrangements. Dr. George Morris Piersol, Philadelphia, President of the College, is in charge of the program of general sessions.

The clinical week is so outlined that clinics, demonstrations, ward-walks, etc., will be given during each forenoon in Chicago's chief hospitals, medical schools and laboratories. The afternoons and evenings will be devoted to general sessions. Sixty eminent authorities from the United States and Canada have been selected to present papers dealing with recent trends in the diagnosis and treatment of disease.

Following the first evening session, Monday, April 16, there will be a Smoker at which a program both entertaining and instructive has been arranged. Dr. H. C. Raven, Associate Curator of the American Museum of Natural History, New York City, will present a lecture with motion pictures and a demonstration of a trained chimpanzee.

The Annual Convocation for the induction of newly elected Fellows will take place Wednesday evening. The chief addresses will be delivered by Dr. George Morris Piersol, President of the College, and by Dr. Grant Fleming, Director of the Department of Public Health and Preventive Medicine, McGill University.

On Thursday evening, April 19, the Annual Banquet of the College will be held. Dr. Glenn Frank, President of the University of Wisconsin, will be the guest speaker.

OPENING GENERAL SESSION

Monday Afternoon, April 16, 1934

2:00 O'CLOCK

GRAND BALLROOM, PALMER HOUSE

1. Addresses of Welcome:
James B. Herrick, General Chairman of the Eighteenth Annual Clinical Session.
Austin A. Hayden, President of the Chicago Medical Society.
Irving S. Cutter, on behalf of the Chicago Medical Schools.

2. Response to Addresses of Welcome:
George Morris Piersol, President of the American College of Physicians.

3. Arteriolar Infarction.
Jonathan C. Meakins, Montreal, Que.

4. Malaria Therapy in Asymptomatic Neurosyphilis.
Paul A. O'Leary, Rochester, Minn.

5. Bronchoscopy in Pulmonary Disease: Its Present Status as an Aid in Diagnosis and Treatment.
Gabriel Tucker, Philadelphia, Pa.

6. Diaphragmatic Hernia.
Carl A. Hedblom, Chicago, Ill.

7. Observations on the Diagnosis and Treatment of Peripheral Vascular Disease.
Eugene M. Landis, Philadelphia, Pa.

8. Hepatic Function in Relation to Hepatic Pathology.
Frank C. Mann, Rochester, Minn.

SECOND GENERAL SESSION

Monday Evening, April 16, 1934

8:00 O'CLOCK

GRAND BALLROOM, PALMER HOUSE

Presiding Officer

JAMES ALEX. MILLER, NEW YORK, N. Y.

1. Development and Disappointments in Blood Studies.
Roger I. Lee, Boston, Mass.

2. The Tuberculosis of Childhood.
Charles Hendee Smith, New York, N. Y.

3. The Permanent Nature of Various Acute Infections.
Allen K. Krause, Tucson, Ariz.

4. Therapeutic Pneumothorax in Experimental Lober Pneumonia in Dogs.
Simon S. Leopold, Philadelphia, Pa.

5. Virus Diseases of Animals Transmissible to Men.
Karl F. Meyer, San Francisco, Calif.

10:20 O'CLOCK

SMOKER

RED LACQUER ROOM, PALMER HOUSE

An unusual program of entertainment, both amusing and instructive, has been arranged.

THIRD GENERAL SESSION

Tuesday Afternoon, April 17, 1934

2:00 O'CLOCK

GRAND BALLROOM, PALMER HOUSE

Presiding Officer

ERNEST B. BRADLEY, LEXINGTON, KY.

1. Energy Exchange in the Study and Management of Disease.
 L. H. Newburgh, Ann Arbor, Mich.
2. Leucopenia in Tuberculosis with Report of a Case Showing a Complete Neutropenic Episode for One Week—Recovery.
 Charles H. Cocke, Asheville, N. C.
3. Newer Clinicopathologic Considerations of the Monocyte and Monocytic Leucosis.
 Charles A. Doan and Bruce K. Wiseman, Columbus, Ohio.
4. The Diagnosis and Management of Certain Types of Chronic Diarrhea.
 Philip W. Brown, Rochester, Minn.
5. Small Intestinal Intubation: Experiences with a Double-Lumined Tube.
 T. Grier Miller and W. Osler Abbott, Philadelphia, Pa.
6. The Criteria of Alcohol Intoxication with Special Reference to 3.2 Beer.
 A. J. Carlson, Chicago, Ill.

INTERMISSION

7. The Rights of the Tuberculous Patient.
 Francis M. Pottenger, Monrovia, Calif.
8. Metabolic Stimulants (Sodium Dinitrophenol).
 Edward L. Bortz, Philadelphia, Pa.
9. Surgical Treatment of Pulmonary Tuberculosis.
 Ralph C. Matson, Portland, Ore.
10. Allergic Diseases in General Practice.
 Harry B. Wilmer and Merle Miller, Philadelphia, Pa.
11. Institutional Treatment for the Chronic Invalid and Convalescent.
 Elmer L. Eggleston, Battle Creek, Mich.

FOURTH GENERAL SESSION

Tuesday Evening, April 17, 1934

8:00 O'CLOCK

GRAND BALLROOM, PALMER HOUSE

Presiding Officer

ARTHUR R. ELLIOTT, CHICAGO, ILL.

1. The Encephalitis Epidemic in St. Louis.
 David P. Barr, St. Louis, Mo.
2. Results of Further Studies on the Physiology of the Anterior Pituitary.
 J. B. Collip, Montreal, Que.
3. Treatment of Angina Pectoris and Congestive Heart Failure by Total Ablation of the Thyroid in Patients without Thyrotoxicosis.
 Herrman L. Blumgart, Boston, Mass.
4. Studies of Cell Potencies and Some Relations to Neoplasia.
 Stanley P. Reimann, Philadelphia, Pa.
5. Biliary Dyskinesia.
 A. C. Ivy, Chicago, Ill.
6. Hematogenous Pulmonary Tuberculosis.
 James Alex. Miller, New York, N. Y.

FIFTH GENERAL SESSION

Wednesday Afternoon, April 18, 1934

2:00 O'CLOCK

GRAND BALLROOM, PALMER HOUSE

Presiding Officer

JAMES G. CARR, CHICAGO, ILL.

1. The Recent Trend Towards a Differentiation Between Allergy and Immunology, and the Relationship to Clinical Medicine.
 Lay Martin, Baltimore, Md.
2. An Explanation of the Mechanism of Infantile Paralysis Production in the Human.
 John A. Toomey, Cleveland, Ohio.
3. A Critical Discussion of the Etiological Factors in Arterial Hypertension.
 Soma Weiss, Boston, Mass.
4. Remarks on the Diagnosis of Coronary Occlusion.
 Louis Hamman, Baltimore, Md.
5. Cutaneous Tuberculosis and Its Relationship to General Medicine.
 Francis E. Senear, Chicago, Ill.

INTERMISSION

6. The Complement Fixation Test as a Guide in the Treatment of Chronic Diseases Resulting from Focal Infections.
 A. F. Jennings and S. W. Wallace, Detroit, Mich.
7. Glycogen Formation in Diabetes.
 F. D. W. Lukens, Philadelphia, Pa.
8. Trends in Diet in Diabetes.
 R. T. Woodyatt, Chicago, Ill.
9. The Diabetic Child.
 Henry J. John, Cleveland, Ohio.
10. Alkalosis: A Clinical Problem.
 Charles T. Way and Edward Muntwyler, Cleveland, Ohio.
11. Certain Bases of Physical Therapy.
 Thomas P. Sprunt, Baltimore, Md.
12. Acquired Heart Block with Adams-Stokes Attacks Dependent Upon a Congenital Anomaly (Persistent Ostium Primum): Report of a Case.
 Wallace M. Yater, Washington, D. C.; Chas. W. Barrier, Fort Worth, Tex., and Paul E. McNabb, Washington, D. C.

ANNUAL CONVOCATION

Wednesday Evening, April 18, 1934

8:00 O'CLOCK

GRAND BALLROOM, PALMER HOUSE

The general profession and the general public are cor-

dially invited. No special admission tickets are required.

1. Convocation Ceremony.
2. Address: "The Medical Aspects of National Health Insurance."
 Grant Fleming, Director of the Department of Public Health and Preventive Medicine, McGill University, Montreal, Que.
3. Presidential Address.
 George Morris Piersol, Philadelphia, Pa.

PRESIDENTIAL RECEPTION

RED LACQUER ROOM

The Reception will follow immediately after the program. Newly inducted Fellows should sign the Roster and secure their Fellowship Certificates during the interim between the Convocation and the Reception.

DANCING

SIXTH GENERAL SESSION

Thursday Afternoon, April 19, 1934

2:00 O'CLOCK

GRAND BALLROOM, PALMER HOUSE

Presiding Officer

JONATHAN C. MEAKINS, MONTREAL, QUE.

1. Further Studies on Granulopenia with Report of Fifteen Additional Cases.
 Stewart R. Roberts and Roy R. Kracke, Atlanta, Ga.
2. Non-painful Features of Coronary Occlusion.
 S. Marx White, Minneapolis, Minn.
3. Classification of Vascular Disease with Special Reference to Etiology, Pathological Anatomy and Pathological Physiology.
 Nathan S. Davis, III, Chicago, Ill.
4. Blood Pressure Variations as a Guide to Treatment and Prognosis.
 Clarence L. Andrews, Atlantic City, N. J.
5. The Early Recognition of Mycardial Disease.
 Walter L. Bierring, Des Moines, Iowa.
6. The Use of Verodigen (a Digitalis Glucoside) in Cardiovascular Disease: Its Pharmacological Assay and Effects on Animals.
 W. D. Stroud, A. E. Livingston, A. W. Bromer, J. B. Vander Veer and G. C. Griffith, Philadelphia, Pa.

INTERMISSION

7. Cardiovascular Observations in 215 Neurosyphilitics.
 Clough T. Burnett and Charles A. Rymer, Denver, Colo.
8. Influential Factors in Recovery from Rheumatoid Arthritis.
 Russell L. Cecil, New York, N. Y.
9. Creatine Metabolism and Blood Cholesterol as Aids in the Diagnosis and Treatment of Hypothyroidism in Children.
 Julius H. Hess, Chicago, Ill.

The Annual General Business Meeting of the College will be held in the Red Lacquer Room immediately after the last paper. All Masters and Fellows are urged to attend. Official reports from the Executive Secretary and Treasurer will be read; new Officers, Regents and Governors will be elected, and the President-elect, Dr. Jonathan C. Meakins, will be inducted into office.

Thursday Evening

8:00 O'CLOCK

GRAND BALLROOM, PALMER HOUSE

THE ANNUAL BANQUET OF THE COLLEGE

(Procure Tickets at the Registration Bureau)

Toastmaster: James B. Herrick, Chicago, Ill.

Address: "The Renewal of America."

Dr. Glenn Frank, President of the University of Wisconsin.

FINAL GENERAL SESSION

Friday Afternoon, April 20, 1934

2:00 O'CLOCK

GRAND BALLROOM, PALMER HOUSE

Presiding Officer

JAMES H. MEANS, BOSTON, MASS.

1. THE UNITED STATES PHARMACOPOEIA XI. Its Relation to Internal Medicine and the Scientific Nature of Its Revision.
 Virgil E. Simpson, Louisville, Ky.
2. The Treatment of Lung Abscess.
 Frederick T. Lord, Boston, Mass.
3. Evaluation of Methods for Testing the Functional Capacity of the Liver.
 William J. Kerr, San Francisco, Calif.
4. Abdominal Pain: Its Significance and Diagnostic Value.
 Thomas R. Brown, Baltimore, Md.
5. Diseases of the Nervous System Producing Dysfunction of Other Organs, and Dysfunction of Other Organs Producing or Simulating Diseases of the Nervous System.
 Lewis J. Pollock, Chicago, Ill.
6. The Blood Sedimentation Test: The Value of Its Use as a Routine, Especially in Pulmonary Tuberculosis.
 Paul H. Ringer, Asheville, N. C.
7. The Thymus and Status Thymico-Lymphaticus.
 A. Graeme Mitchell, Cincinnati, Ohio.

INTERMISSION

8. Undulant Fever.
 Joseph L. Miller, Chicago, Ill.
9. Personality Study in the Practice of Internal Medicine.
 Edward Weiss, Philadelphia, Pa.
10. A Study of Ten Cases of Bronchomoniliasis.
 John W. Flinn, Robert S. Flinn and Zebud M. Flinn, Prescott, Ariz.
11. Factors Influencing Operative Mortality in Hyperthyroidism.
 Willard O. Thompson, S. G. Taylor, III, and Karl A. Meyer, Chicago, Ill.
12. The Interrelationship of Renal and Gastrointestinal Disease.
 Harry Gauss, Denver, Colo.

Who's Who in the Editorial Council

CLINICAL MEDICINE
DISEASES OF DIGESTION

ABRAHAM HIGHAM AARON,

Associate Professor of Medicine and Therapeutics, University of Buffalo Medical School. Attending Physician, Buffalo General Hospital. 40 North Street, Buffalo, New York.

WALTER CLEMENT ALVAREZ, M.D.,

Associate Professor of Medicine, University of Minnesota (Mayo Foundation). Mayo Clinic, Rochester, Minnesota.

ALBERT FREDERICK RUGER ANDRESEN, M.D.,

Clinical Professor of Medicine (Gastroenterology) Long Island College of Medicine. Attending Physician (Gastroenterology) Long Island College Hospital. Chief of Gastroenterological Service, Polhamus Memorial Clinic, Brooklyn. Chairman, Section on G.E. and Proctology, A.M.A. 88 6th Ave., Brooklyn, New York.

J. ARNOLD BARGEN, B.S., M.S. IN MED., M.D.,

Assistant Professor of Medicine, Mayo Foundation, University of Minnesota. Consultant in Medicine, Mayo Clinic, Rochester, Minn. Intestinal hospital service at St. Marys Hospital, Rochester, Minn. Mayo Clinic, Rochester, Minn.

JOHN MINOR BLACKFORD,

Chief of Medical Division, Virginia Mason Hospital and Clinic, Seattle, Wash.

LEON BLOCH, M.D.,

Ass't Clinical Professor Medicine, Rush Medical College. Attending Physician, Michael Reese Hospital. Attending Physician, Cook County Hospital 1906 to 1920. 310 S. Michigan Ave., Chicago, Illinois.

ARTHUR LEONARD BLOOMFIELD,

Professor of Medicine and Executive Head of Division of Medicine, Stanford University School of Medicine. San Francisco, Calif.

RUSSELL SAGE BOLES, M.D.,

Associate in Medicine, University of Pennsylvania. Visiting Physician to the Philadelphia General Hospital. Consulting Gastro-Enterologist, U.S. Veterans Bureau, Philadelphia. Rittenhouse Plaza, Philadelphia, Pa.

HENRY L. BOCKUS, M.D.,

Professor of Gastro-Enterology, Graduate School of Medicine, University of Pennsylvania. Attending Gastro-Enterologist, Graduate Hospital, University of Pa. Physician in charge of Department of Gastro-Enterology, Bryn Mawr and Abington Memorial Hospitals. 250 South 18th Street, Philadelphia, Pa.

HARLOW BROOKS, M.D.,

Emeritus Professor of Clinical Medicine, University of Bellevue Hospital Medical College. Attending Physician, Bellevue Hospital. Consulting Physician French Hospital, St. Vincents, Fifth Avenue, Polyclinic, Beth Israel, Greenwich Hospital, Mt. Vernon Hospital, St. Johns Hospital, Yonkers, South Side Hospital, Vassar Brothers Hospital, Poughkeepsie, etc. 47 West 9th Street, New York, N. Y.

THOMAS RICHARDSON BROWN, M.D.,

Associate Professor of Medicine, Johns Hopkins University. Physician in charge Division of Digestive Diseases, Johns Hopkins Hospital. Visiting Physician, Union Memorial Hospital, Hospital for the Women of Maryland, Church Home and Infirmary. Member of: Association of American Physicians, American Gastro-Enterological Association, American Medical Association, Maryland Medical and Chirurgical Faculty. 12 East Eager Street, Baltimore, Maryland.

WILLIAM FITCH CHENEY,

Clinical Professor of Medicine (Emeritus), Stanford University, School of Medicine, San Francisco, Calif.

EDGERTON L. CRISPIN,

Attending Physician, Los Angeles County Hospital, Los Angeles, Calif.

BURRILL B. CROHN, M.D.,

Instructor, Post-Graduate Medicine, Columbia University. Associate in Medicine, Mt. Sinai Hospital. Consultant Gastro-Enterologist, Rockaway Beach Hospital. 1075 Park Avenue, New York, N. Y.

PROF. JOSEPH EDMOND DUBE, M.D., F.R.C.P., F.A.C.P., CHEVALIER DE LA LEGION D'HONNEUR.

Professor of Clinical Medicine at l'Universite de Montreal. Physician to the Hotel-Dieu Hospital, Montreal. Membre correspondant de la Societe Medicale de Paris. President of "La Societe d'Alimentation et de Gastro-enterologie" de Montreal. 454 Sherbrooke Street East, Montreal, P. Q., Canada.

ELMER LESLIE EGGLESTON, M.D., F.A.C.P.,

Chief of Gastro-Enterological Section, The Battle Creek Sanitarium. Battle Creek Sanitarium, Battle Creek, Michigan.

G. B. EUSTERMAN, M.D.,

Head of Section in Medicine, Mayo Clinic. Chief of Clinic Services in Diseases of the Digestive System. Associate Professor of Medicine, University of Minnesota, Mayo Foundation. Attending Physician, St. Mary's and Colonial Hospitals. Mayo Clinic, Rochester, Minnesota.

JULIUS FRIEDENWALD, M.D.,

Professor of Gastro-Enterology, University of Maryland. Visiting Gastro-Enterologist to the University, Union Memorial, Mercy, Church Home and Infirmary, Women's and Sinai Hospitals, Baltimore. Trustee of the Institute for Advanced Study, Princeton, N. J. 1013 N. Charles Street, Baltimore, Maryland.

ERNEST HOWARD GAITHER, M.D.,

Associate in Medicine, Johns Hopkins University, Baltimore. Member: American Medical Association, American Gastro-Enterological Association, Southern Medical Association, American College of Physicians, Medical and Chirurgical Faculty of Maryland. Visiting Physician Johns Hopkins Hospital, Union Memorial Hospital, Church Home and Infirmary, Hospital for the Women of Maryland, Bon Secours Hospital. 12 East Eager Street, Baltimore, Maryland.

R. H. M. HARDISTY, M.D.,

Lecturer in Medicine, McGill University. Assistant Physician, Royal Victoria Hospital. 814 Medical Arts Bldg., Montreal, Canada.

ALLAN A. JONES,

Professor of Clinical Medicine, School of Medicine, University of Buffalo, Buffalo, New York.

CLEMENT RUSSELL JONES, M.D., F.A.C.P.,

Professor of the Principles of Medicine, University of Pittsburgh Dental School. Visiting Physician Mercy Hospital, Presbyterian Hospital, Mayview Hospital, Falk Clinic, Pittsburgh, Pa. 1102 Empire Building, Pittsburgh, Pa.

NOBLE WILEY JONES,

Professor of Medicine, School of Medicine, University of Oregon, Portland, Ore.

SARA M. JORDAN, M.D.,

Gastro-Enterologist, Lahey Clinic, New England Baptist Hospital Staff, New England Deaconess Hospital Staff. 605 Commonwealth Ave., Boston, Mass.

JOSEPH WILLIAM LARIMORE, A.B., M.D., F.A.C.P.,

Associate Professor of Clinical Medicine, Washington University Medical School. Assistant Radiologist for Gastro-Enterology, The Edward Mallinckrodt Institute of Radiology, Washington University Medical School. 617 Beaumont Medical Bldg., St. Louis, Mo.

JEAN ROGER ARTHUR LESAGE, M.D., B.A.,

Assistant in Medicine and Chief of the Gastro-Intestinal Division, St. Luke's Hospital, Montreal. Joint Secretary of the "Societe scientifique d'Alimentation et de Gastro-enterologie", Montreal. Secretary for Canada at the "Gazette Medicale de Paris," France, and of the French-speaking Countries. Second Secretary of the "A.D.R.M." (Canada). Member of the Editorial Staff of the review: "L'Union Medicale du Canada". 418 Sherbrooke St. East, Montreal, Canada.

B. B. VINCENT LYON, A.B., M.D., Sc.D., F.A.C.P.,

Assistant Professor of Medicine, Jefferson Medical College. Assistant Physician, Jefferson Hospital. Chief of Clinic, Gastro-Intestinal Department of Curtis Clinic, Jefferson Hospital. 2031 Locust Street, Philadelphia, Pa.

CHARLES MARTIN,

Dean, Faculty of Medicine, Magill University, Montreal, Canada.

LAY MARTIN, M.D.,

Associate in Medicine, Johns Hopkins University. Assistant Visiting Physician, Johns Hopkins University. 1201 N. Calvert Street, Baltimore, Maryland.

JOHN GASTON MATEER,

Physician in Charge, Gastro-Intestinal Division, Henry Ford Hospital (since 1920). Graduated from Johns Hopkins Medical School in 1918. Henry Ford Hospital, Detroit, Michigan.

WM. GERRY MORGAN, A.B., M.D., Sc.D., LL.D.,

Regent of Georgetown University. Dean of the Department of Medicine, Professor of Gastro-Enterology, Physician to Georgetown University Hospital. Consultant to Garfield Hospital and Gallinger Municipal Hospital. 1801 Eye Street, Washington, D. C.

FRANCIS D. MURPHY, M.S., M.D.,

Professor Medicine and Director of the Department of Internal Medicine, Marquette University School of Medicine. Medical Director of Milwaukee County General Hospital. 536 West Wisconsin Avenue, Milwaukee, Wisconsin.

MOSES PAULSON, B.S., M.D., F.A.C.P.,

Member of American Gastro-Enterology Association, American Society of Bacteriologists. Associate in Medicine, Johns Hopkins University. Assistant Visiting Physician, Johns Hopkins Hospital, also Visiting Physician, Gastro-Intestinal Division of the Medical Clinic, and member of the Medical Staff (Gastro-Enterology) of the Diagnostic Clinic of the Johns Hopkins Hospital. Medical Arts Building, Baltimore, Maryland.

GEORGE MORRIS PIERSOL, M.D., B.S.,

Professor of Medicine, Graduate School of Medicine of the University of Pennsylvania. Physician to the Graduate School Hospital. Physician-in-Chief, Abington Memorial Hospital. Active Consultant in Medicine, Philadelphia General Hospital. 1913 Spruce Street, Philadelphia, Pa.

MARTIN REHFUSS,

Clinical Professor of Medicine (Gastro-Enterology), Jefferson Medical College, Philadelphia, Pa.

VERNON C. ROWLAND, M.D.,

Associate Professor Western Reserve University, at present mainly in Dental College. Formerly in Medical College and still lectures by invitation. May do more teaching later. Visiting Physician St. Luke's Hospital, in charge of Gastro-Intestinal Clinic. 7016 Euclid Avenue, Cleveland, Ohio.

LEON SCHIFF, M.D.,

Assistant Professor of Medicine, University of Cincinnati Medical School. Assistant Attending Physician, Medical Service, Cincinnati General Hospital. Director, Gastrointestinal Clinic, Cincinnati General Hospital. 408 Doctors Bldg., Cincinnati, Ohio.

HOWARD FRANCIS SHATTUCK, M.D.,

Professor of Medicine, N. Y. Post-Graduate Medical School of Columbia University. Attending Physician, N. Y. Post-Graduate Hospital. 33 East 68th Street, New York, N. Y.

SIDNEY K. SIMON, M.D.,

Professor Gastro-Enterology, Graduate School, and Associate Professor Clinical Medicine, School of Medicine, Tulane University, New Orleans. Chief of Gastro-Intestinal Service, Touro Infirmary, New Orleans. Visiting Physician, Baptist Hospital, New Orleans. 1520 Aline Street, New Orleans, Louisiana.

VIRGIL E. SIMPSON, M.D.,

Professor Clinical Medicine, Medical School, University of Louisville. Member of Staffs of Norton Infirmary and Louisville City Hospital. Consultant Internal Medicine Kosair Crippled Children's Hospital and Masonic Widows and Orphans' Home, Louisville, Ky. 1100 Francis Building, Louisville, Kentucky.

HORACE W. SOPER, M.D.,

Staff: St. Lukes Hospital, De Paul Hospital, Jewish Hospital. 3701 Westminster Place, St. Louis, Missouri.

CYRUS CRESSEY STURGIS, M.D.,

Professor of Internal Medicine, University of Michigan Medical School. Director, Thomas Henry Simpson Memorial Institute for Medical Research. Director, Department of Internal Medicine, University Hospital. Simpson Memorial Institute, Ann Arbor, Michigan.

MARTIN G. VORHAUS, M.D.,

Associate Attending Physician, Hospital for Joint Diseases. Chief of the Medical Clinic, Hospital for Joint Diseases. 145 West 58th Street, New York, N. Y.

HARRY GILMER WALCOTT, M.D., F.A.C.P.,

Emeritus Professor of Gastro-Enterology, Baylor University College of Medicine. Member Staff Baylor University Hospital. Graduate Baltimore Medical College 1901. Associate Professor of Clinical Pathology, Baltimore Med. College 1901-2; Professor of Gastro-Enterology, Southwestern University Med. College 1904-1911; Professor Gastro-Enterology Southern Methodist University Medical College 1911-1915; Professor Gastro-Enterology Baylor University College of Medicine, 1914-1950. 1424 Medical Arts Bldg., Dallas, Tex.

LUTHER FISKE WARREN, A.B., M.D., F.A.C.P.,

Professor of Medicine, Long Island College of Medicine. Physician-in-chief, Long Island College Hospital & St. John's Hospital. Medical Director, Brooklyn Home for Consumptives. Consulting Physician, Methodist Episcopal Hospital, Harbor Hospital, Brooklyn, South Side, Bay Shore, Brunswick General, Amityville. 200 Hicks Street, Brooklyn, N. Y.

FRANKLIN W. WHITE, M.D.,

Consulting Physician, Boston City Hospital. Instructor, Post-Graduate Courses, Harvard Medical School. 322 Marlborough Street, Boston, Mass.

L. G. ZERFAS,

Associate Professor of Medicine, Indiana University, Chief Clinician, Indianapolis City Hospital.

NUTRITION

CLIFFORD JOSEPH BARBORKA, B.S., M.S., Sc.D., M.D., F.A.C.P.,

Instructor in Medicine, Northwestern University Medical School. Formerly Consultant Physician, Mayo Clinic 1921-1932. Passavant Memorial Hospital. 700 N. Michigan Avenue, Chicago, Ill.

REGINALD FITZ, M.D.,

Associate Professor of Medicine, Harvard Medical School. 721 Huntington Avenue, Boston, Mass.

E. B. FREEMAN, M.D.,

Associate in Clinical Medicine, Johns Hopkins University. Assistant Visiting Physician, Johns Hopkins Hospital. Physician-in-chief, Maryland General Hospital. Gastro-Enterologist, Saint Agnes' Hospital. Attending Physician, Bon Secour Hospital. Attending Physician, Church Home and Infirmary. 807 Cathedral Street, Baltimore, Maryland.

SEALE HARRIS, M.D.,

Professor Emeritus of Medicine, University of Alabama. Visiting Physician, Birmingham Baptist Hospital, Birmingham, Ala. Care of Seale Harris Clinic, Highland Ave. at Sycamore St., Birmingham, Ala.

HENRY J. JOHN, M.D.,

Head of Diabetic Department and Laboratories at Cleveland Clinic for the last 13 years. (Only private practice at present). 10515 Carnegie Avenue, Cleveland, Ohio.

HOWARD FRANK ROOT, M.D.,

Assistant in Medicine Courses for Graduates, Harvard Medical School. Physician, New England Deaconess Hospital, Boston. 81 Bay State Road, Boston, Mass.

FREDERICK F. TISDALL, M.D., F.R.C.P., (C)., FELLOW, AMERICAN ACADEMY OF PAEDIATRICS,

Director, Research Laboratories and Assistant Physician, Hospital for Sick Children. Associate in Paediatrics, Department of Medicine, University of Toronto. 67 College Street, Toronto, Ontario, Canada.

PARASITOLOGY

WILLIAM C. BOECK, M.D., F.A.C.P., FELLOW A.M.A., ASSOCIATE, AMERICAN COLLEGE OF GASTROENTEROLOGY

Associate Prof. of Medicine, College of Medical Evangelists, Los Angeles. Senior Attending Physician, Los Angeles County General Hospital, Los Angeles. Visiting Physician to Hollywood Hospital and The Good Samaritan Hospital, Los Angeles. Member Malignancy Board, Los Angeles County General Hospital, Los Angeles. 1709 West 8th Street, Los Angeles, California.

CHARLES F. CRAIG, M.D., M.A., F.A.C.P., F.A.C.S.,

Colonel, U. S. Army, Retired. Professor o Tropical Medicine and Head of the Department of Tropical Medicine, Medical School of Tulane, University of Louisiana, New Orleans, La. Medical School, Tulane University, 1430 Tulane Ave., New Orleans, Louisiana.

ROBERT HEGNER, M.D., PH.D.,

Professor of Protozoology, Johns Hopkins University, School of Hygiene & Public Health. 615 N. Wolfe St., Baltimore, Maryland.

KENNETH MERRILL LYNCH, M.D., LL.D.,

Professor of Pathology, Medical College of the State of So. Carolina. Pathologist to the Roper Hospital, Charleston, So. Carolina. Consulting Pathologist to various hospitals of So. Carolina. Medical College of the State of So. Carolina, Charleston, South Carolina.

THOMAS BYRD MAGATH, M.D.,

Section on Clinical Pathology (Consulting Physician), Mayo Clinic. Associate Professor of Pathology and Parasitology, Mayo Foundation, Graduate School of Medicine, University of Minnesota, Rochester, Minn. Editor, American Journal of Clinical Pathology. Mayo Clinic, Rochester, Minnesota.

H. MELENEY,

Professor of Pathology (Parasitology), Vanderbilt University, School of Medicine, Nashville, Tenn.

ABDOMINAL SURGERY

IRVIN ABELL, M.D.,

Professor Clinical Surgery, University of Louisville Medical School. Staff Surgeon, Louisville City Hospital and St. Joseph Infirmary. Consulting Surgeon, Children's Free Hospital and Kosair Crippled Children's Hospital. Member: American Medical Association, Southern Medical Association, American College of Surgeons, American Surgical Association, Southern Surgical Association, American Gastro-Enterological Association, American Urological Association. 321 W. Broadway, Brown Building, Louisville, Kentucky.

(Continued on Page 90)

ALBERT A. BERG, M.D.,

Surgeon to Mt. Sinai Hospital, New York City. Director of Surgery, Montefiore Hospital, New York, and Beth Moses Hospital, Brooklyn. Consulting Surgeon, Monmouth Memorial Hospital, Long Island, Hebrew Sheltering Orphan Asylum, Brooklyn, Barnet Memorial Hospital, Paterson, N. J., etc. 10 East 73rd Street, New York, N. Y.

THE HON. HERBERT ALEXANDER BRUCE, M.D., L.R.C.P., F.R.C.S. (Eng.),

Emeritus Professor of Surgery and Member of Board of Governors of the University of Toronto. LL.D. University of Toronto; Queen's University; Western University. Consulting Surgeon, Toronto General Hospital. Lieutenant-Governor of the Province of Ontario. Government House, Toronto, Ontario, Canada.

LESTER R. DRAGSTEDT, M.D., PH.D.,

Professor of Surgery, The University of Chicago. Attending Surgeon at the Albert Merritt Billings Memorial Hospital. Department of Surgery, University of Chicago, 950 East 59th Street, Chicago, Illinois.

JOHN MILLER TURPIN FINNEY,

Professor of Surgery Emeritus, Johns Hopkins University. Consulting Surgeon of Johns Hopkins Hospital, Union Memorial Hospital, Church Home & Infirmary, Hospital for the Women of Maryland, Sinai Hospital. Chief Consultant in Surgery to the A.E.F. Decorations received: D.S.M. United States; Commandeur de l'Ordre de la Couronne, Belgium; Officer de la Legion d'Honneur, France. 3119 St. Paul St., Baltimore, Maryland.

CHARLES GORDON HEYD, B.A., M.D., F.A.C.S.,

Professor of Surgery, N. Y. Post-Graduate Medical School, Columbia Univ. Director of Surgery, N. Y. Post-Graduate Medical School, Columbia Univ. Consulting Surgeon, Woman's Hospital, New York City. 116 East 53rd Street, New York, N. Y.

FRANK LAHEY,

Surgeon-in-Chief, Lahey Clinic, Boston, Mass.

DEAN LEWIS,

Professor of Surgery and Head of the Department of Surgery, Johns Hopkins University, Medical School, Baltimore, Maryland.

J. TATE MASON, M.D.,

President of the Virginia Mason Hospital Corporation. Chairman of the Board of The Mason Clinic. The Mason Clinic, Virginia Mason Hospital Bldg., Seattle, Washington.

RUDOLPH MATAS, M.D., Sc.D., LL.D., F.R.C.S. Eng. (Hon.),

Emeritus Professor of Surgery, Medical School, Tulane University. Chief, Surgical Division, Touro Infirmary, New Orleans Consulting Surgeon, Charity Hospital, New Orleans. 2255 St. Charles Avenue, New Orleans, Louisiana.

EDWARD WILLIAM ALTON OCHSNER, M.D.,

Professor of Surgery, Tulane University School of Medicine, New Orleans. Visiting Surgeon, Charity Hospital and Touro Infirmary, New Orleans. Consulting Surgeon, Illinois Central Hospital, New Orleans. 1430 Tulane Avenue, New Orleans, Louisiana.

N. M. PERCY,

Professor of Clinical Surgery, School of Medicine, University of Illinois, Chicago, Illinois.

JAMES TAFT PILCHER,

Professor of Clinical Surgery, Long Island Hospital, College of Medicine, Brooklyn, N. Y.

CHARLES T. STURGEON, M.D.,

Member of: Pacific Coast Surgical Association, Western Surgical Association, American College of Surgeons, California State Medical Association, American Medical Association, also local medical societies. Clinical Professor of Surgery, Medical School, Univ. of So. California. Director and Chief Surgeon, Good Hope Hospital Association. Senior Attending Surgeon, Los Angeles General Hospital. Surgical Staff of the Hospital of the Good Samaritan, St. Vincent's Hospital, Cedars of Lebanon Hospital. 1930 Wilshire Blvd., Los Angeles, California.

Who's Who in the Editorial Council — *continued*

ROENTGENOLOGY

DAVID S. BEILIN, M.D.,

Director of Radiological Department, Augustana Hospital, Chicago. 411 Garfield Avenue, Chicago, Illinois.

JAMES THOMAS CASE, M.D.,

Professor of Radiology, Northwestern University Medical School. Surgeon, Grant and Edgewater Hospitals. Radiologist, Passavant and Evanston Hospitals. Editor, Annals of Roentgenology. Consultant in Radiology, Cook County Hospital. 180 N. Michigan Avenue, Chicago, Illinois.

ARTHUR C. CHRISTIE, M.D.,

Consultant in Radiology, Veteran's Bureau, Washington, D. C. 1835 Eye Street, N. W., Washington, D. C.

BYRL RAYMOND KIRKLIN, M.D.,

Associate Professor of Radiology and Director of the Division of Radiology, Mayo Foundation, University of Minnesota Graduate School and Head of Section of Roentgenology, Mayo Clinic. Mayo Clinic, Rochester, Minnesota.

WILLIAM H. STEWART, M.D.,

Visiting Physician, Lenox Hill Hospital in charge of Roentgen Dept. Clinical Professor Roentgenology, Post-Graduate School Medical Department, Columbia College. Lenox Hill Hospital, 107 East 76th Street, New York, N. Y.

OESOPHAGUS

CHEVALIER JACKSON, M.D., Sc.D., LL.D., F.A.C.S.,

Professor of Bronchoscopy and Esophagoscopy, Temple University. Consultant in Department of Bronchoscopic Research, Temple University. 3432 North Broad Street, Philadelphia, Pa.

PORTER PAISLEY VINSON, M.D.,

Associate Professor of Medicine, The Mayo Foundation Graduate School, University of Minnesota. Mayo Clinic, Rochester, Minnesota.

SURGERY OF THE LOWER COLON AND RECTUM

LOUIS ARTHUR BUIE, B.A., U. OF S. C., 1911, M.D., U. OF MD., 1915, F.A.C.S., F.A.P.S., SIGMA XI,

Head of Section on Proctology, Mayo Clinic, Associate Professor of Surgery, University of Minnesota (Mayo Foundation). Mayo Clinic, Rochester, Minnesota.

CLEMENT R. MARTIN, M.D.,

Clinical Professor of Proctology, Loyola University School of Medicine, Chicago. Chief of the Proctologic Clinic, Mercy Hospital, Chicago. Attending Proctologist to Municipal Tuberculosis Sanitarium, Chicago, and The Hines Memorial Hospital for World's War Veterans, Hines, Ill.

JEROME MORLEY LYNCH, M.D., F.A.C.S.,

Professor of Proctology, New York Polyclinic. Formerly Surgical Director of St. Bartholomew's Hospital, New York. Surgeon St. Mary's, Hoboken, Broad Street Hospital, New York. Cons. Surgeon Neurological Institute, Medical Center, New York; N. J. State, Saranac Lake & Mary Thompson, Torrington, Conn. Member A.M.A., N. Y. Academy of Medicine; American Gastro-Enterological Association; American Proctologic Association; Military Order Foreign Wars. Author: "Diseases of Rectum and Colon"; "Tumor of the Colon and Rectum"; Contributor Johnson's Surgery, Wood's Hand Book of Medical Sciences, Tice's Practice of Medicine. 205 E. 61st Street, New York, N. Y.

CURTICE ROSSER, M.D., F.A.C.S.,

Professor of Proctology, Baylor University College of Medicine. Proctologist, Baylor and Parkland Hospitals. 710 Medical Arts Building, Dallas, Texas.

EXPERIMENTAL PHYSIOLOGY

BORIS P. BABKIN, M.D. (ST. PETERSBURG), D.Sc. (LONDON), F.R.S.C.,

Research Professor of Physiology, McGill University, Montreal, Can. Department of Physiology, Biological Building, McGill University, Montreal, Canada.

FREDERICK GRANT BANTING, M.C., M.B., M.D., D.S.C., F.A.C.P.,

Professor of Medical Research, University of Toronto. Banting Institute, University of Toronto, Toronto, Canada.

A. J. CARLSON, PH.D., M.D., Sc.D.,

Professor of Physiology, University of Chicago. Department of Physiology, University of Chicago, Chicago, Illinois.

ANDREW CONWAY IVY, M.D.,

Nathan Smith Davis Professor of Physiology and Pharmacology, Northwestern University Medical School. Northwestern University Medical School, 303 E. Chicago Avenue, Chicago, Illinois.

THERAPEUTICS

WALTER A. BASTEDO, PH.G., M.D., Sc.D., F.A.C.P.,

Asst. Professor of Clinical Medicine, Columbia University. Consulting Physician, St. Luke's Hospital, New York, Staten Island Hospital and St. Vincent's Hospital, Staten Island. President, United States Pharmacopoeial Convention 1930-1940. (Formerly Curator of the New York Botanical Garden. Instructor in Pharmacology, Cornell University. Associate in Pharmacology and Therapeutics, Columbia University. Member Advisory Council, New York Dept. of Health. Attending Physician, St. Luke's and City Hospitals). 33 East 68th Street, New York, N. Y.

HARRY BECKMAN, M.D.,

Professor and Director, Department of Pharmacology, Marquette University School of Medicine. Marquette University School of Medicine, Milwaukee, Wisconsin.

ALLERGY

WARREN T. VAUGHAN, M.D.,

Editor, Journal of Laboratory and Clinical Medicine. Asst. Editor, Journal of Allergy. Secretary-Treasurer, Association for the Study of Allergy. 808 Professional Bldg., Franklin Street at 5th, Richmond, Virginia.

Business Office:
435-455 Lincoln Bank Tower
Fort Wayne, Indiana

BEAUMONT S. CORNELL
Supervising Editor

AMERICAN JOURNAL OF
DIGESTIVE DISEASES AND NUTRITION
435-455 Lincoln Bank Tower
Fort Wayne, Indiana

Editorial Office:
920 North Michigan Avenue
Chicago, Illinois

FRANK SMITHIES
Editor-in-Chief

Editorial Council

CLINICAL MEDICINE—DISEASES OF DIGESTION

Abraham Higham Aaron, *Buffalo, N. Y.*
Walter Clement Alvarez, *Rochester, Minn.*
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CHRONIC ULCERATIVE ENTERITIS*

By
PHILIP CORR, M.D.
and
WILLIAM C. BOECK, M.D., F.A.C.P.
LOS ANGELES, CALIFORNIA

FROM a group of inflammatory lesions involving the small bowel Crohn, Ginzberg and Oppenheimer (1) have recently extracted a clinical and pathological entity which they term "regional ileitis." Harris, Bell and Brunn (2) subsequently reported three similar cases and called this new disease "chronic cicatrizing enteritis." The purpose of our paper is to describe a similar case having noteworthy features under the more inclusive name of "chronic ulcerative enteritis."

Essentially, this disease occurs in young adults as a subacute or chronic ulcerative lesion of unknown etiology confined rather sharply to the small bowel with a pronounced tendency to cicatrization and stenosis. Clinically, it simulates in many ways chronic ulcerative colitis.

The investigators cited above have designated four types of this disease but we prefer to regard them as *phases* since they are all progressive stages of *one* disease process. These *four phases* of chronic ulcerative enteritis are, (1) *the early phase*, characterized by an insidious onset with intraabdominal inflammatory symptoms which may become more severe and simulate acute appendicitis except for its slower onset and its progression into the chronic stages. (2) A *chronic phase*, characterized by more or less severe ulcerative enteritis with recurrent moderate diarrhea and abdominal cramps. (3) A *later phase*, characterized by stenoses which produce obstructive symptoms. This phase is the one most commonly encountered. (4) A *fourth phase*, characterized by persistent fistulae which occur spontaneously between loops of bowel or appear late, postoperatively, as abdominal fistulae such as may follow appendicectomy or subsequent to enteroanastomosis.

Our patient presents noteworthy features in regard to long duration of the ailment (six years), its complication, apparently by amebic infection, a possibility which was not considered in the differential diagnosis by the above authors, extensive, progressive, ulcerative involvement of the ileum and jejunum and by the existence of marked pseudo-polyposis located between ulcerating areas of mucosa.

CASE HISTORY

Mrs. O. E. D., aged 30, housewife, presented herself August 29, 1932 for advice concerning the continuance of antiamebic treatment.

Her past history disclosed an attack of typhoid fever in 1912 following which she was unusually well and strong until May 1927, one year after the birth of her third child; then began the present symptoms of intestinal cramps and diffuse intestinal soreness associated with alternate diarrhea and constipation. The intestinal soreness had been practically constant for five years with considerable variation in intensity, worse when the diarrhea occurred at which times the dull soreness would give way to severe cramp-like pains of short duration; these would "double her up." Diarrhea, up to seven or eight stools daily, of a watery character without obvious pus, blood or mucus at any time alternated with periods of mild constipation during these five years. By the end of the first year, the patient had decreased from her average weight of 100 pounds to 75 pounds.

After considerable consultation an appendicectomy had been performed on May 30, 1928, because it was considered that she had an appendicitis due to amebic infection, amebae previously having been found in her stools. *At operation*, a chronic obliterative appendix was found and the bowel was said to have been "reddened and diseased." With subsequent rest, tonic medication and much antiamebic treatment the patient regained considerable strength during the next six months. Then the alternating diarrhea and mild constipation, the abdominal cramps and diffuse soreness, and the loss of weight and strength recurred with severity and again after rest and tonic treatment she improved. This cycle of improvement and retrogression had recurred several times so that the patient had become a semi-invalid over the five year period. Along with other antiamebic treatment, when we observed her she had just completed her tenth series of a course of 100 *anayodin* tablets. She felt, for her, unusually well; the abdominal soreness had almost ceased. For the past few weeks, she had been attending to some of her home duties. The family history was entirely negative for tuberculosis.

Physical examination revealed a thin woman with a pasty complexion, a malar flush and with a temperature of 98.7, pulse 71, blood pressure 114/80, weight 97 pounds. General examination was negative except for a diffuse, mild tenderness in the lower abdomen and the feeling of a sense of resistance in the right fornix on vaginal examination although no definite mass could be made out. There was an appendicectomy scar.

Three stool examinations were negative for blood, parasites or ova. The *hemoglobin* was 78%, with 4,100,000 erythrocytes and 8,200 leucocytes. A *gastric analysis* revealed normal acids. The *Wassermann* was negative. A *stereoscopic roentgenogram* of the chest was negative. Further observation and at least a temporary cessation of antiamebic treatment with a continuance of a program of curtailed exertion and a smooth high calorie, high vitamin diet were advised.

SECOND STUDY: The patient did not return for five months. By February 1, 1933, diarrhea had gradually increased to four to seven stools daily. Her weight dropped from 97 pounds to 83 pounds. Three attacks of abdominal cramping pain had occurred associated with vomiting, each lasting a day or two. The patient became markedly emaciated and dehydrated. Tenderness was noted in the right lower quadrant and it was felt vaginally that the bowel could be palpated in the right fornix. A tight fibrous ring was observed inside the rectum. The temperature was 98.5, blood pressure 104/60, pulse 96. Otherwise the examination was essentially negative as previously described. An unsatisfactory *proctoscopic examination*, for a distance of 15 cm., revealed a slightly reddened mucous membrane with a small ulcer just inside the ring. Smears were taken from the ulcer but on examination no amebae or cysts were found. In two of four stool examinations, a very occasional cyst of *Endameba hystolytica* was seen. There was no blood or pus in the specimens. A few *Endameba coli* cysts also were seen. The hemoglobin was 75% with 4,524,000 erythrocytes and 7,200 leucocytes.

Progress: Eleven grains of emetin and 4.5 grams of *treparsol* were given over a two week period without definite change in the condition. The temperature ranged from subnormal to 100.6°. The weight had dropped to 79 pounds. By May 16, however, her weight increased to 81 pounds.

On May 29, 1933, another attack of cramping pains occurred; this was accompanied by vomiting. Definite small bowel peristalsis became visible; the abdominal wall had a doughy feel. An immediate operation for the relief of the suspected obstruction was advised. It was felt, preoperatively, that the lesion was a chronic intestinal obstruction, the primary lesion probably being tuberculous (as a cause of the diarrhea) and this or possibly postoperative adhesions following the appendicectomy was producing obstruction. X-ray studies of the gastro-intestinal tract were not considered advisable because of the obstructive signs and symptoms.

At operation, the surgeon felt a small mass in the cecum. The terminal six inches of the ileum were normal. The ileum, proximal to this, was large, "wet" and hose-like; a red inflamed linear area was prominently exhibited in the serosa. There were a few white, longitudinal girdle scars throughout the involved bowel; these caused stenosis with almost complete obstruction, the uppermost scar was about three feet distal to the pylorus. The intestine was divided five inches above the ileocecal valve and the ends were closed. A lateral anastomosis from a relatively normal portion of the upper ileum was made to the ascending colon. A second lateral anastomosis from the jejunum to the transverse colon was made after the discovery of a more proximal obstruction. Five days postoperatively, a recto-vaginal fistula developed; this persisted until the patient died. Twenty-five days postoperatively, the incision broke down and a fecal-fistula developed. With so many leaks and so little remaining intestinal absorbing-surface, the patient succumbed to inanition and infection July 20, 1933, seven and one-half weeks postoperatively and six years after the onset of symptoms.

PATHOLOGY

The autopsy (limited to the abdomen) was performed by Dr. George D. Maner. Grossly, the intra-abdominal appearance was that noted at the operation with the addition of multiple ventral fistulae from the

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breakdown of all the anastomoses. The blind ends of the terminal ileum, however, had not broken down. The colon was devoid of all pathology except for the small recto-vaginal fistula (which was identified but not examined further) and a very superficial ulceration, 3 cm. in diameter, in the cecum from one edge of which originated a small benign polypoid mass (Figure 1). The ileocecal valve and the distal five inches of the ileum were devoid of pathology. The remaining portion of the small



Figure 1. Gross specimen of cecum showing large shallow ulcer and *polypoid mass. Terminal ileum free of ulceration.*

bowel, with the exception of the proximal three feet, was largely the location of ulcers of varying size, depth and shape, separated by bridges of swollen mucosa and the presence of polypoid masses (Figure 2). Scars were numerous and in a few places these had caused marked constriction of the bowel producing almost complete obstruction. There was some

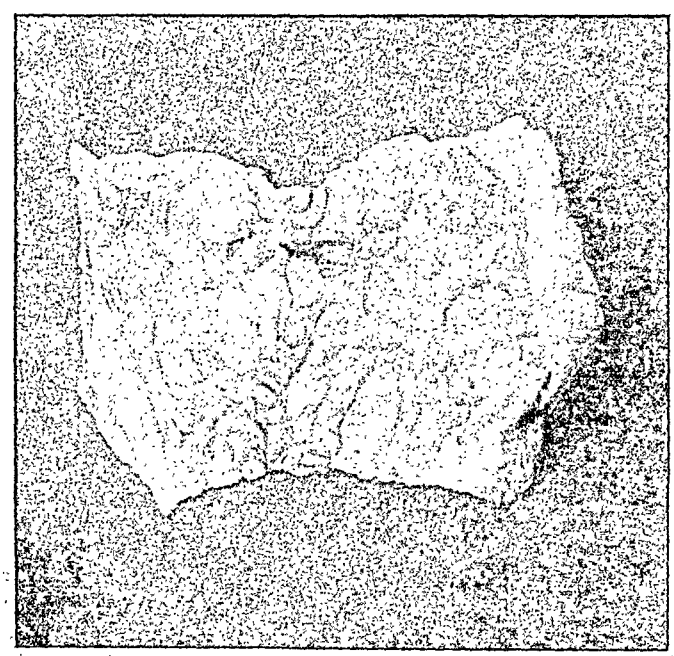


Figure 2. Gross specimen from ileum showing many typical ulcers and pseudopolyposis.

undermining of the edges of the ulcers and of the scarred areas. The bowel wall was thickened, particularly in the submucosal elements. The regional glands were normal. The other abdominal organs essentially were normal.

Microscopically, the most striking feature was the almost complete absence of the epithelium of all of the diseased small intestine (Figure 3).

In some places there was evidence of *metaplasia*: a flat pavement-like or cuboidal epithelium had replaced the glandular epithelium (Figures



Figure 3. Section from ileum showing deep ulceration, edema, and almost total absence of epithelium.

4 and 5), but generally there was very little evidence of epithelialization; instead, there was a loss of all glandular structures.

The submucosal coats were edematous and in the muscular layers the swelling had produced marked separation and lamination of the muscle fibers (Figures 3 and 4). The blood vessels were congested in some areas and empty in others. There was no evidence of free hemorrhage but small deposits of hemosiderin were noted in the submucosa. There was a tendency to dilatation of the lymphatics.

There was considerable plasma-cell infiltration coincident with a scattering of eosinophiles and neutrophiles (Figure 5). Giant cells were encountered occasionally but none were of the Langhans' type.



Figure 4. Section from ileum showing ulceration, edema, and metaplasia of epithelium.

Peyer's patches seemed to have been destroyed and replaced by scars and localized thickening of the submucosal coats causing a tendency to stenosis. Rarely, one encountered a solitary lymph follicle; when present, it showed destructive changes and marked replacement by the infiltrating plasma-cells.

The ulcers were both shallow and deep. The shallow ulcers were characterized by destruction of the epithelium and submucosa lying above the *muscularis mucosae*. The deep ulcers penetrated to or into the *muscularis* (Figures 3 and 4). No evidence of perforation was observed.



Figure 5. High power magnification of rectangular area marked in Figure 4 showing pavement-like epithelium, edema and infiltration chiefly by plasma cells.

The pathologic picture in no way resembled tuberculosis; amebae were not found in the tissues. It was apparent that the process was one of progressive ulceration with little or no evidence of repair. As in those cases previously described in the literature, microscopic study failed to contribute anything capable of explaining the etiology of this disease.

COMMENT

We believe that this report adds another case to the group of cases so brilliantly isolated and described by Crohn, Ginzburg and Oppenheimer. These observers called the disease "regional ileitis" because the pathology in their cases was chiefly limited to lesions involving the ileum and the ileocecal valve. Harris, Bell and Brunn felt that their cases belonged to the disease described but that the involvement of the jejunum in one of their cases made the term "regional *ileitis*" inapplicable. In our case too, the normal Bauhin's valve and the normal terminal ileum and the extensive involvement of the jejunum would make it seem that the term "regional ileitis" is too limited. One might as well designate the disease now known as "chronic ulcerative colitis" as "chronic ulcerative proctitis" because the pathology is most evident in the rectum, as to call this ulcerative disease of the small bowel by the name of "regional *ileitis*."

Harris, *et al*, objected to "regional ileitis" and named the disease "chronic cicatrizing enteritis" because cicatrization was such a prominent characteristic of the lesion. The contributions of both groups of observers, however, referred to the cicatrization and resulting stenosis as being only a *later phase or stage* of the disease which complication gives rise to an obstruction demanding urgent surgical intervention. But it would appear that it should be possible to diagnose the affection earlier than in its stenotic phases. We feel therefore that the name "chronic cicatrizing enteritis" like "regional ileitis" also limits too considerably the scope of the described pathology of the disease, but admit the difficulty of suggesting a more accurate or inclusive phrase.

We feel that the basic pathology in this disease is ulceration; its chronicity produces a picture not unlike that seen in the colon in instances of "chronic ulcerative colitis" as described by Bargen. Therefore we suggest (because of its comprehensiveness) the name "chronic ulcerative enteritis."

As in the cases previously reported, no etiological agent was found. Pathologically, tuberculosis was somewhat simulated but none of the giant cells were of the typical Langhans' type; no glandular involvement occurred nor was tuberculosis found elsewhere on clinical examination including an X-ray study of the chest. Seemingly, lues could be excluded by the history of three normal children, a negative Wassermann and the absence of other associated history facts or clinical and pathological findings.

Amebiasis as the cause of the lesions was repeatedly suggested throughout the clinical course. At intervals during the seven years, *Endameba histolytica* had been found in the stools and considerable treatment had been directed toward this infection. At autopsy attention was drawn by the pathologist to the undermined edges of the ulcerations as an indication of amebic etiology. Against the amebic etiology of the ulcers might be listed the following: 1. amebic enteritis above the ileum is not recorded in the literature; 2. the colon and the lower part of the ileum were practically free of involvement; 3. the constricting, scarred, stenotic lesion is not a feature of amebic pathology; 4. polypoid growths associated with ulcers of amebic origin have not been described; 5. epithelialization, characteristic of healed, amebic ulcerations was not in evidence; 6. no "crusting," diphtheritic membrane characteristic of amebic infection was seen; 7. the extensive ulcerations if of amebic etiology should ordinarily have revealed amebic pathology elsewhere in the colon and possibly a liver abcess; 8. the history of watery diarrhea with no pus or blood is not characteristic of amebic dysentery; 9. finally, microscopically, no evidence of amebae were found in the ulcers. Therefore we feel that, clinically, the case did not conform to an amebic dysentery and that, pathologically, amebiasis could be excluded as an etiological factor. It is our opinion that amebiasis was an incidental, secondary infection, and it had been cleared up by adequate and appropriate treatment.

The clinical course was remarkable because of its duration (six years) and because it ran the course of the four different phases mentioned in our classification given above. The ulcerative phase occurred early; it was followed by symptoms simulating subacute appendicitis for the relief of which appendicectomy was performed. Then came a long history of recurrent, incomplete obstructions of the small bowel to be followed, finally, by multiple, late postoperative fistulae.

Pathologically, the striking features of this case included the freedom from ulcerations or of other lesions of the terminal ileum; involvement of all but about three feet of the small bowel: the marked, diffuse pseudopolyposis surrounded by ulcerating areas such as has been reported in cases of chronic ulcerative colitis, and the continued activity of the disease as evidenced by the red, subacutely inflamed, linear areas in the thickened, "wet" submucosa and serosa.

Recognized in its early phases, the affection should, by surgical resection, frequently have the benign outcome as emphasized by Crohn, *et al* and obtained in one of three cases reported by Harris *et al*. Early diagnosis should be made preoperatively by a survey of the early signs and symptoms and by a thorough X-ray investigation of the small intestine. At the operating table, the pathology should be recognized by the characteristic lesions which have been described by others and in this communication.

SUMMARY

A case of "chronic ulcerative enteritis" has been described. The term "chronic ulcerative enteritis" is, we believe, preferable to the more limited terms, "regional ileitis" and "chronic cicatrizing enteritis."

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GASTRIC SECRETION FOLLOWING IRRADIATION OF THE EXPOSED STOMACH AND THE UPPER ABDOMINAL VISCERA BY ROENTGEN RAYS*

By

ALBERT M. SNELL, M.D., *Division of Medicine,*

and

JESSE L. BOLLMAN, M.D., *Division of Experimental Medicine,*
The Mayo Clinic
ROCHESTER, MINNESOTA

DURING the past two decades a number of experimental observations have been made upon the effect of irradiation of the stomach with reference both to anatomic changes so produced and to alterations in gastric secretion which may follow.

All observers agree that in adequate doses irradiation produces definite morphologic changes in the stomach's mucosa as well as temporary decreases in the quality and quantity of gastric secretion. These results have led to a consideration of the possible use of roentgen therapy in peptic ulcer, on the theory that a more or less prolonged depression of gastric secretory function should have a beneficial effect upon the healing of benign inflammatory or of ulcerative gastric lesions. The actual results of such treatment have been variable, possibly because of biologic differences among patients studied and differences in the roentgenologic technic exhibited. The present study was undertaken with the idea of reviewing the experimental basis for such treatment and of studying the possibilities of its clinical application.

The *literature on this subject* recently has been fully reviewed by Desjardins, by Nicolesco and his co-workers, and by Viviani, so that a further critical analysis seems unnecessary. The studies of Ivy and his collaborators, however, being most recent and complete, therefore, deserve particular attention. These investigators irradiated dogs, who had Pavlov pouches, with 160 per cent of the erythema dose for the dog, which dose is approximately four times the erythema dose for the human subject. Irradiation of this degree produced gastric hyposecretion with achylia, which condition persisted for about three or four weeks; during the period of recovery, the gastric acids returned to normal concentrations, but not to volumes secreted. The secretion of pepsin was greatly reduced; the secretion of chlorides was unaltered. Morphologic studies[2] of these animals indicated permanent injury of a considerable degree to the gastric mucosa. Ivy and his collaborators concluded that the effect of irradiation upon gastric secretion was direct and that other extraneous factors definitely could be excluded. Their results, which may be regarded as a standard, do not differ materially from those of earlier workers. Desjardins, in summarizing the evidence on the sensitivity of the stomach to roentgen rays, concluded that it is considerably less sensitive than is the small intestine, and that the degree and duration of the effect on secretion depend to a great extent on the *dose* of roentgen rays used and the *number* and *frequency* of treatments. He found no evidence for the theory that small doses of roentgen rays act as stimulants to gastric secretion and he agreed that the secretory variations observed are due to a direct destructive effect on the gastric mucosa. The clinical effects, according to both Desjardins and Viviani, are variable and inconstant, depending also upon the dose, on biologic differences among patients and on levels of gastric acidity which existed before treatment was begun.

PURPOSE OF THIS STUDY

Although it is admitted that the artificial production by roentgen therapy of partial destruction of the gastric mucosa in order to cause anacidity or hyposecretion is not, of itself, desirable, it is certainly no less so than are the extensive surgical procedures required to control symptoms among patients who habitually exhibit recurrent peptic ulcers. Among certain of these patients the tendency to formation of ulcer cannot be controlled by rigid medical management nor by conservative surgical treatment. It is in this type of case that, even after radical gastric resection, there is an abnormally highly acid gastric secretion and a persistent tendency to formation of ulcer. Irradiation with resultant atrophy of the mucosa might be the lesser of two evils. For this reason, in this study of the effect of irradiation on gastric secretion, we have attempted to apply methods of experimentation to the dog which might be applicable clinically. This procedure, necessarily, involves the use of a dose of roentgen rays which, while affecting gastric secretion will not produce roentgen cachexia and which will permit the maintenance of good health and nutrition in the animals which are being studied. Also it involves a longer experimental period of observation, since acute, depressing effects on gastric secretion are less important from a clinical standpoint than is the maintenance of long continued hyposecretion. The studies to be reported attempt to meet these requirements. We have followed two lines of procedure: (1) depression of gastric secretion by fractional doses of radiation applied to the *intact upper portion of the abdomen*, with repeated single doses thereafter, and (2) single doses of radiation of the *surgically exposed stomach*, with subsequent irradiation of the intact upper portion of the abdomen. In each instance, both the general state of the animal's nutrition and the levels of gastric acidity were taken as a guide to further treatment. The experimental animals were observed over periods of from nine to fifteen months; studies of the gastric secretions were made at frequent intervals. Morphologic observations of the gastric mucosa also were made of animals which died or were killed as the experiments progressed.

METHODS

Dogs were used in all experiments. During the period of study these animals were maintained on a standard kennel ration, to which corn syrup and milk were added during the period of anorexia which followed irradiation. One animal with a gastric fistula was used; the remainder were normal.

For the study of gastric secretion, a dose of 1 mg. of histamine was administered subcutaneously and gastric juice was collected by stomach tube at fifteen-minute intervals for one to one and a half hours thereafter. Meat meals (80 gm. of ground horse meat and 250 c.c. of water) were given to all animals in about 20 per cent of the tests, chiefly to permit comparison with the results of previous observers.

Before irradiation, each animal was subjected to from five to fifteen or more fractional analyses of gastric secretion, in order to accustom

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them to the test procedure, to obtain an idea of the nature of the individual gastric secretion, and to eliminate the factor of nervous inhibition.

The gastric acidity was determined on the filtered gastric secretion in the usual manner, using a tenth-normal solution of sodium hydroxide, with Topfer's reagent and phenolphthalein as indicators. The hydrogen ion concentration was determined by the Leeds-Northrup potentiometer, using the gold hydroquinone electrode. Pepsin was determined in a few instances by Gilman and Cowgill's modification of Gates' method.

The *roentgen dose employed* varied somewhat with the type of experiment and the size and general condition of the animal. Five standard doses were employed, the details of which are given in Table 1. The

TABLE I

Details of roentgen dosage

Kilovolts Sphere Gap (Peak Kilovolts)	Minimum Wave Length	Milliamperes	Filter	Distance, cm.	Time, Minutes	Roentgens Per Minute	Total Dose (roentgens)
130	0.15A	5	Aluminum 1 mm.	22.5	114	115	13,110
130	0.15A	5	None	22.5	22	278	6,116
130	0.15A	5	Aluminum 2 mm.	22.5	39	77	3,003
130	0.15A	5	Aluminum 2 mm.	22.5	30	77	2,310
130	0.15A	5	Aluminum 3 mm.	22.5	30	64	1,920

one used most frequently was 3,000 *roentgens* (international); this is approximately of the same magnitude as that used by Ivy and his collaborators; it amounts approximately to 150 per cent of the erythema dose for the dog. The largest dose, 13,000 *roentgens*, was used only once; that was in an experiment involving surgical exposure and irradiation of the stomach. In other experiments of this type, from one-quarter to one-half of this dose was employed. In all such experiments, the abdominal viscera were screened from the irradiated field by the use of lead shields, thus eliminating any effect on other organs which might confuse the result. In irradiating the intact animal, the smaller doses mentioned in Table 1 were employed, the rays being directed as a beam into the gastric region. This procedure probably resulted in some irradiation of the intestines, spleen and pancreas. The consequences of this irradiation of other viscera, however, may not have been of great importance, since the general effects of irradiation on gastric secretion were approximately the same in the two groups of cases. Control experiments, involving irradiation of the hind legs, were carried out on one animal with negative results; as other observers have noted, irradiation of the legs, thorax and head does not affect gastric secretion to any significant degree.

RESULTS

The effect of irradiation of the *intact, upper portion of the abdomen* upon the gastric secretion of our animals was somewhat less than that previously recorded by Ivy and his collaborators, although we used a dose of roentgen rays of approximately the same magnitude. The difference may be explained, in part, by the fact that those observers used dogs with Pavlov pouches and confined the irradiation to the pouch and to its immediate vicinity, whereas, in our experiments, irradiation was, for obvious reasons, less accurately localized.

It will be noted that for three dogs the total amount of irradiation required to produce anacidity varied from 5,310 to 11,950 *roentgens*. In the largest animal of the three (dog 1) there was little change in gastric acidity until the final fractional dose of the first course of irradiation was given, but anacidity finally developed which persisted for about three weeks; gastric acidity thereafter never was markedly affected by irradiation (Figure 1). In a smaller animal (dog 3) which received the same total roentgen dose, a reduction in gastric acidity occurred somewhat earlier; almost complete anacidity was maintained for about twice as long a period, and return to normal gastric secretion was slow; in this dog also, a relatively greater effect from subsequent irradiations occurred. In a third animal (dog 4) of approximately the same weight as dog 3, anacidity developed after a total dose of 5,310 *roentgens* and there was evidence of a more severe and lasting disturbance of gastric secretory capacity. These results may best be explained on the basis of biologic differences. It is possible that, with the last dog, the small intestine may have been irradiated to a greater degree than with the other two, since it was the only animal of the group in which diarrhoea developed. The most significant features

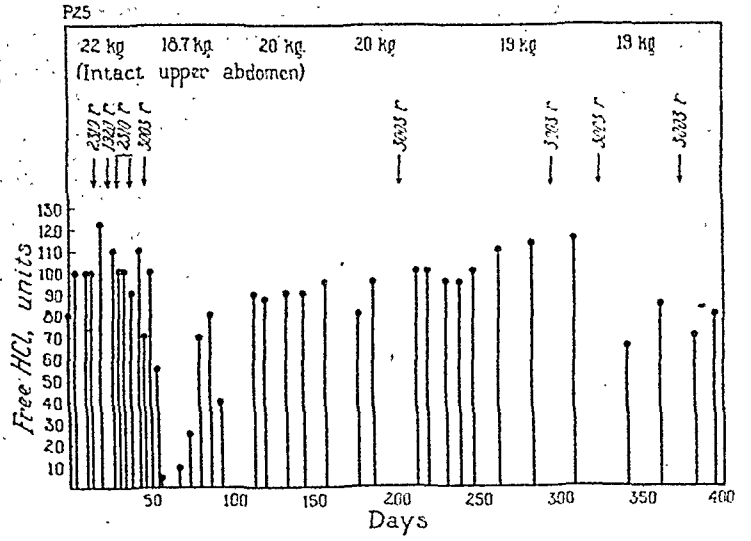


Figure 1 (dog 1). The effect of irradiation of gastric region on levels of free hydrochloric acid in gastric juice. Each line represents the maximal acidity attained by stimulation with histamine on the day designated.

of the experiments on this group of dogs which were *irradiated over the intact abdomen* are: (1) the extremely large doses required to produce anacidity in two animals, (2) the relatively high resistance of the stomach to subsequent irradiation and (3) the low resistance of one animal, possibly because of biologic variation.

The experiments on the second group of animals in which the *exposed stomach was irradiated* are of greater interest, since among these animals, there was no question of any roentgenologic effect on the intestines or other viscera. So far as we are aware, these are the first recorded experiments on irradiation of the exposed and isolated stomach. The resistance of all of these animals to irradiation was so great that some doubt was cast on the nature of depressed gastric secretion reported in certain earlier studies. As Ivy and his co-workers have shown, irradiation of the small intestine, of itself, lowers gastric secretion; it seems that this may be a factor in any reduction of gastric acidity which follows irradiation of the *intact* upper portion of the abdomen. One dog of our series received the huge dose of 13,000 *roentgens* over the exposed stomach and survived eighteen days; normal gastric secretion occurred for four days after operation and complete anacidity did not develop until about a week later.

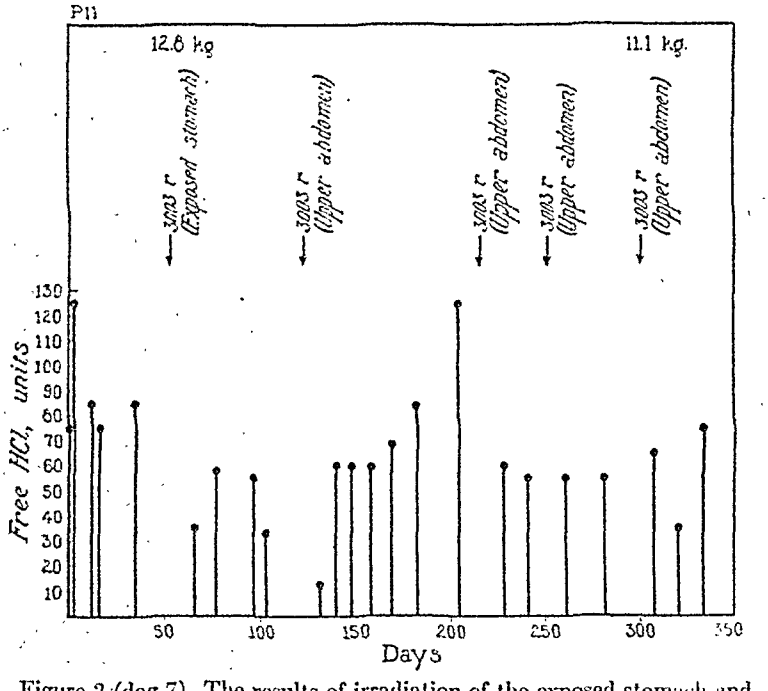


Figure 2 (dog 7). The results of irradiation of the exposed stomach and subsequent irradiation of intact upper portion of abdomen on maximal values for free hydrochloric acid after stimulation with histamine.

A dose of 3,000 *roentgens* over the exposed stomach did not produce anacidity in two other animals, and the same dose over the intact abdomen given later produced no very great change in the gastric acidity of these two animals (Figure 2). One dog tolerated 6,000 *roentgens* over its exposed stomach without obvious systemic effect; anacidity appeared in this animal eighteen days later, and relatively low levels of gastric secretion persisted for about ten weeks. This animal's gastric acidity again was abolished by a second dose of 6,000 *roentgens* over the surgically exposed stomach given about ten and a half months later; previous irradiation over the *intact* abdomen had produced only moderate reductions in gastric

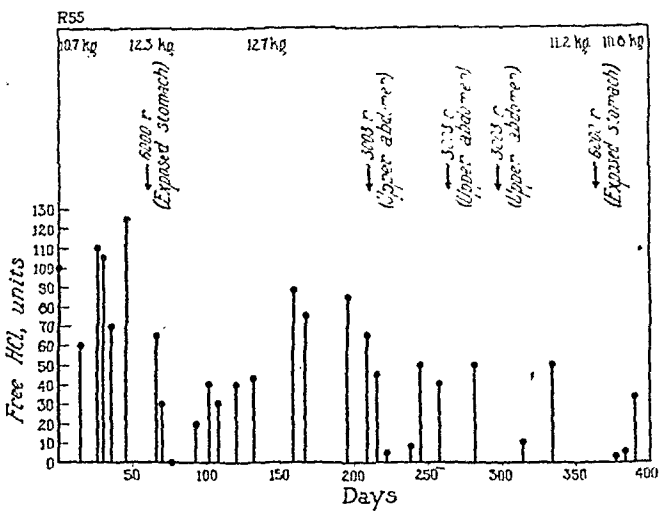


Figure 3 (dog 5). The effect of irradiation of the surgically exposed stomach on the maximal level of free hydrochloric acid obtained by stimulation with histamine.

acidity (Figure 3). Curiously enough, the only animal (dog 2), which of the four so treated showed any ill effects, was given a dose of roentgen rays practically incompatible with life. The other animals, in spite of the effects of anesthesia, the prolonged exposure of the abdominal viscera during the process of irradiation and the relatively large roentgen doses, were not any more affected than were those in the first group in which the rays were directed to the *intact* abdomen.

In both groups of animals, the high resistance to irradiation was not more striking than was the tendency of gastric secretion to be resumed. After variable periods, and to a variable degree, there was a return of gastric acidity toward normal which, in certain animals, persisted in spite of actinodermatitis, loss of weight and cachexia. It was definitely noted, however, that *volumes of secretion were decreased* and that the *duration of secretion* after stimulation with histamine was brief. The total amount of hydrochloric acid secreted by the previously irradiated stomach must, therefore, be considerably less than normal, although single specimens revealed satisfactory concentrations of acid and correspondingly high values for the hydrogen ion concentration.

The *pepsin concentrations* encountered in the gastric juices of these animals after irradiation deserve brief consideration. As the unpublished *data* of Bollman and Osterberg demonstrate, there is considerable variability in the normally high peptic activity of the gastric juice of the normal dog. These variations make it difficult to draw definite conclusions as to the exact effect of irradiation on secretion of pepsin. Pepsin determinations were made at various times following irradiation upon four of the animals in this series. Some of the results are given in Table 2. It will be noted that, in two cases, the pepsin concentration was considerably reduced, although one animal was capable of secreting a considerable quantity of hydrochloric acid after stimulation with histamine. In two other cases, in which the animals had proved to be resistant to the effects of irradiation, the pepsin values

TABLE II

Concentration of pepsin in gastric juice after irradiation of the stomach

Dog	Date	Fasting	15 Minutes	30 Minutes	45 Minutes	1 Hour	1 Hour, 15 Minutes	Maximum Free HCl, Units	Time Since Last Irradiation, Weeks
7	3-1	1300	1375	1275	1225	1250	1325	85	4
	3-8		1500	625	675	1150		83	1
	3-12	2175	2100	1500	1775	3200		58	2
5	2-28	725	810	1050	1275	950		5	2
	3- 8	1150	855	1075	480			10	3
	3-14	3000	1010	2100	3200	2125		38	4
6	3- 8	3575	3075	2050	2175	3050	1675	75	1
	3-13	5600	1750	1460	2600	2450		53	2
1	10-5	1975	2825	2700	1000	3400	510	110	8
	2-28	4200	10500	5750	8700	4050		75	2

were not so greatly altered. Most observers who have determined the peptic activity of the gastric juice after irradiation conclude that it is affected to a lesser degree than is the acid-secreting mechanism and that significant changes are noted only when the hydrochloric acid content of gastric juice is greatly reduced. Our results in general are confirmatory but, because of the known variations in normal animals, the findings should not be regarded as absolutely conclusive.

The effect of irradiation upon the *morphologic characteristics of the gastric mucosa* recently has been studied by Dawson. This material was obtained from the Pavlov pouches of dogs used by Ivy[6] in the experiments to which we referred in an earlier paragraph. The microscopic appearance of the gastric mucosa of our animals corresponds quite closely with that described by Dawson, in spite of differences in the roentgenologic technic employed. Five hours after a single dose of 3,000 *roentgens* over the *intact* upper portion of the abdomen, there was little visible change in the mucosa of the stomach; some edema and leukocytic infiltration were noted in the submucosa and serosa. In another case in which the animal (dog 2) died eighteen days after a dose of 13,000 *roentgens* over the *exposed* stomach, there was marked disorganization and necrosis of the gastric epithelium (Figure 4). The superficial layers and portions of the neck of the gastric glands were completely destroyed. The deeper portions of these glands were partially preserved; each contained a few normal cells situated just above the *muscularis mucosae*. The "chief" cells disclosed relatively greater degree of injury than did the parietal cells. There was no evident formation of new connective tissue and leukocytic infiltration practically was absent.

In two other instances in which the animals (dogs 1 and 3) had received approximately the same total roentgen dose over a longer period of time, the histologic picture indicated a destructive process of a more chronic nature (Figure 5). In both animals, there was definite atrophy of the mucosa; this was reduced about 50 per cent in thickness. The superficial layers of mucous epithelium were partially preserved especially in their deeper portions. The crypts of the gastric glands greatly were reduced in depth; portions of the neck of these glands disclosed the most extensive destruction and, in many regions, almost were completely destroyed. The chief cells were poorly preserved, and in many of those which remained, granules of zymogen were not apparent. The parietal cells were less affected and in many places stood out prominently. Whatever increase in connective tissue there may have been probably was more apparent than real, and resulted from the destruction of so large a number of epithelial elements of the mucosa. Leukocytic infiltration was almost entirely absent.

In one case in which the animal (dog 4) had been irradiated so long as about nine months before its death and in which a considerably reduced gastric secretion had occurred thereafter without further irradiation, a somewhat different histologic appearance was noted (Figure 6). Sections from this animal revealed almost complete destruction of the

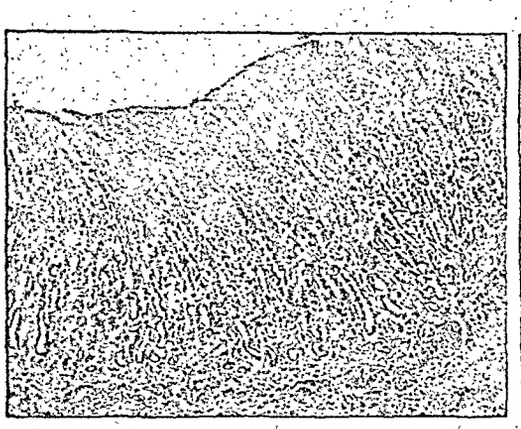


Figure 4 (dog 2). The destructive effect of a large single dose of roentgen rays over the surgically exposed stomach.

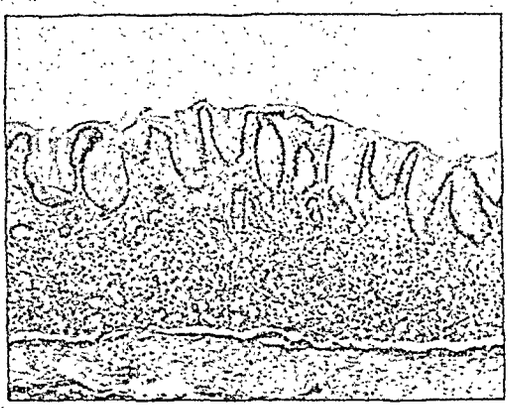


Figure 5 (dog 1). The effect of repeated irradiation of intact upper portion of abdomen on the gastric mucosa. There is relative thinness of the mucosa and disorganization of its structure.

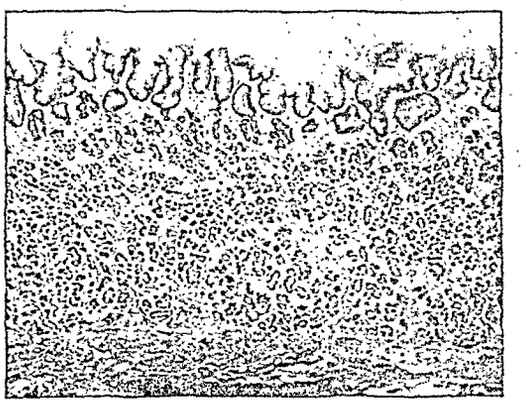


Figure 6 (dog 4). The appearance of gastric mucosa nine months after irradiation. There is possibly some regeneration of the parietal cells.

"chief" cells, especially those of the neck of the gastric glands. The parietal cells were numerous, indicating either resistance to irradiation or regeneration. The superficial epithelium was normal throughout, but the total thickness of the mucosa greatly was reduced. Immediately below the superficial epithelium, there was some evidence of fibrosis; there was an increase in the collagenous fibrils of the submucous coat. Leukocytic infiltration was almost entirely absent and there was no appreciable change in the blood vessels. In all sections the "chief" and neck cells appeared to be most greatly affected; the parietal cells appeared more resistant, a finding which doubtless explains the restoration of acidity of the gastric juice even after heavy irradiation. In this dog, the general appearance of the gastric mucosa suggested a reparative process in which the parietal cells were regenerating. In none of the sections studied by us did atrophy and destruction of the mucosa approximate that seen in the stomachs of clinical subjects affected with pernicious anemia or with other diseases associated with a *true, permanent achylia gastrica*.

COMMENT

From our experiments, one may conclude that any substantial or lasting reduction in gastric acidity requires for its production a dose of roentgen rays just short of that which produces fatal roentgenologic cachexia. Heavy irradiation of the surgically exposed stomach, while relatively well-tolerated, did not always produce complete anacidity and reductions in acidity were at best only of short duration. Repeated irradiation of the intact abdomen was relatively less effective and, in addition, led to the formation of actinodermatitis of various degrees among certain animals. These experiments indicate again the relative insensitivity of the stomach to irradiation and the tendency of gastric secretion to be resumed even after serious injury to the gastric mucosa. After observing our experimental animals over a period of a year or more, and considering the massive doses of roentgen rays required to produce transient reductions in secretion, it seems unlikely that irradiation of the stomach offers any prospect of controlling hyperacidity and hypersecretion in man. When more conservative doses were employed at longer intervals and the animals were kept in satisfactory condition, reductions in acidity were scarcely sufficient to warrant the difficulties involved. Even if roentgenologic treatment of corresponding degree was feasible in clinical cases, it seems doubtful whether reductions in acidity of the degree and duration accomplished in these experiments would be of much therapeutic value in human peptic ulcer subjects. Such reductions could be obtained by less radical methods, and in fact have repeatedly been accomplished in other ways without curative effect.

The conservative doses of roentgen rays used by those who have recently attempted roentgen therapy for gastric hypersecretion in man[8] have been much smaller than those required to produce any significant effect in animals. Even such effects as have been described are slight and of short duration. It may be argued that a pathologic degree of hypersecretion might be affected to a greater extent, but this has not been the experience of those who have studied roentgenologic effects in clinical subjects (Viviani). In some of the reported studies on roentgenologic effects in man, the reduction in acidity occurred so soon after irradiation and returned to normal within such brief periods that the effects noted possibly were psychic rather than physical.

Among patients affected with ulcer, the relief from symptoms following radiotherapy is difficult to interpret; it may be attributed in some instances to the spontaneous remissions so common in all types of peptic ulcer. In one recent communication, the relief of pylorospasm by irradiation is suggested[8]. As Desjardins has pointed out, symptomatic improvement of patients with ulcer reported by some observers may be due not so much to a diminution of gastric secretion or acidity as to an action on the local infiltration of leukocytes, which is a common feature in peptic ulcer. Our studies, as well as those of Dawson, on the morphologic appearance of the gastric mucosa after irradiation indicate the plausibility of such an explanation: in practically all sections studied, leukocytes virtually were absent. Another possible hypothesis has to do with the effect of irradiation on pepsin concentration, which, while inconstant, might conceivably affect certain patients with ulcer in whom peptic activity has been shown to be greatly increased.

SUMMARY

1. Irradiation of the intact upper portion of the abdomen of dogs produces a variable and temporary reduction in gastric acidity and a definite destructive effect on gastric mucosa. It is not possible to maintain a consistently low level of acidity for any prolonged period without the production of actinodermatitis or "radiation sickness."

2. Irradiation of the surgically exposed and isolated stomach produces a similar effect on gastric secretion which effect also is temporary. Larger single doses of roentgen rays are required to produce such an effect. Subsequent irradiation of the intact upper portion of the abdomen of these animals reduces gastric acidity but permanent anacidity has not been attained by this means.

3. There is evidence to indicate a considerable variation in radiosensitiveness of different animals, which variation does not increase with repeated irradiation.

4. It is suggested that the reported symptomatic improvement of patients affected with ulcer who have received irradiation by roentgen rays may be due to an effect on local leukocytic infiltration rather than to a direct effect on gastric secretion.

PROTOCOLS

Dog 1. A male pointer, weighing 19.7 kg., had been used in previous studies on gastric secretion. A gastric fistula, made with a loop of ileum according to the method of Mann and Bollman, had been established in November, 1931. January 17, 1933, studies preliminary to irradiation were begun. The animal then weighed 22 kg. and was in good condition. After five histamine meals, and one meat meal, a dose of 2,310 *roentgens* was given over the intact upper portion of the abdomen January 30. Prior to irradiation, free hydrochloric acid to the amount of 100 units repeatedly was noted with pH values of 1.3 to 1.4. Two days after irradiation, the animal appeared normal and, with the usual stimulation with histamine, the maximal acid values were 125 free hydrochlroic acid and 135 total acidity. A second irradiation (1,920 *roentgens*) was given over the upper portion of the abdomen February 6; on February 9, the maximal free hydrochloric acid value after stimulation with histamine was 110 units. February 13, a third irradiation was given (2,310 *roentgens*). This and all subsequent doses were given over the intact upper portion of the abdomen. The following day the dog was apathetic and sick, but the maximal levels of gastric acidity were essentially unchanged on February 14, 16 and 21. February 22, a fourth irradiation (2,310 *roentgens*) was given; three days later, there was still no change in gastric secretory ability; on February 28, the first significant decrease in gastric acidity (a maximal value of 70 units of free hydrochloric acid after stimulation with histamine) was noted. March 1, a fifth dose (3,000 *roentgens*) was administered. Gastric secretion was normal on March 4; by March 8 a marked decrease in total quantity of secretion and in gastric acidity was noted (maximal acid values 45 free hydrochloric acid, and 60 total acidity). On March 10 and 14, with histamine and with meat test meals, respectively, there was no free hydrochloric acid; the animal was in poor condition but weighed 20 kg. March 21, the dog seemed to be improving, but anacidity persisted after stimulation with histamine. A week later, there was a small amount of free acid, and test meals at weekly and biweekly intervals until August 7 revealed a gradual increase in gastric secretory capacity; the pre-irradiation levels, however, were not attained. A dose of 3,000 *roentgens* (August 7), produced no significant effect, although the animal's gastric secretions were examined regularly until November 7. During this entire period the dog was in excellent condition, averaging about 1 kg. under its greatest recorded weight. On November 7, December 8 and February 1, respectively, 3,000 *roentgens* were administered; after the last two doses, reductions in gastric acidity were observed and the animal appeared to be failing rapidly in strength. February 1, an area of actinodermatitis was noted on the anterior abdominal wall. February 23, the dog's condition was not good, but after stimulation with histamine a free hydrochloric acid value of 95 units was noted with a pH of 1.31. The following day, the animal was sacrificed; on gross examination all the abdominal viscera appeared normal. The gastric mucosa had a curious dry, moth-eaten appearance suggesting atrophic gastritis.

To conserve space, some of the following protocols have been condensed.

Dog 2: A male mongrel, weighing 11.2 kg., was given 13,110 *roentgens* over the surgically exposed stomach. The dog survived eighteen days, was in good condition for about two weeks, and anacidity did not appear until eleven days after irradiation. At necropsy, the gastric mucosa was congested and edematous; microscopic sections disclosed practically complete necrosis of the superficial mucosal layer.

Dog 3: A female shepherd, weighing 11 kg., was given a total of 11,950 *roentgens* in five fractional doses over a period of four weeks. These were given over the intact upper portion of the abdomen. Anacidity developed six days after the last dose and persisted for about four weeks. Meat test meals and stimulation with histamine thereafter revealed a gradual resumption of gastric secretory activity, but pre-irradiation levels never were attained although the animal was in good general condition and maintained its weight. A dose of 3,000 *roentgens* was given on August 8, November 1, and December 7, respectively, each dose being followed by a period of decrease in gastric secretion and then by a subsequent increase. The animal was sacrificed February 14. At necropsy, the surface of the stomach showed whitish patches indicating peritoneal irritation. The walls of the small intestine appeared somewhat thinner than normal, but were otherwise not remarkable. The gastric mucosa presented grossly an appearance suggesting atrophic gastritis.

Dog 4: A male mongrel terrior, weighed 11.6 kg. After the usual period of observation to establish the normal level of gastric secretion, the animal was given an irradiation of 2,310 *roentgens* and 3,000 *roentgens* on February 22 and March 1, 1933, respectively; both were given over the intact upper portion of the abdomen. These procedures were followed by marked systemic effect with anorexia and loss of weight; eight days after the last irradiation, anacidity developed which persisted for five weeks. The dog was followed for ten months; there was a partial return of the gastric secretion, but neither the quantity nor concentration of acid returned to normal. On August 8 and August 25, there was virtually complete anacidity without obvious cause; the animal's weight had returned to normal and it appeared healthy. Fairly normal acid secretion appeared again October 13; a third dose of 3,000 *roentgens* was given November 2, and this was followed by actinodermatitis and the animal was sacrificed. Grossly, the findings at necropsy were not remarkable.

Dog 5: A male bull terrier, weighing 12.3 kg. was subjected to the usual training period; seventeen test studies of gastric secretion after stimulation in the histamine were made over ten weeks. Values for free hydrochloric acid averaged about 100 units, with occasional higher levels of acidity (free hydrochloric acid 125 units, and a pH of 1.17 on one occasion). March 31, the abdomen was opened with the animal under ether anesthesia. The stomach was drawn out and isolated on all sides by lead shields; all other abdominal viscera were screened by the same method. A single dose of 6,116 *roentgens* (unfiltered) was given in twenty-two minutes and the abdomen closed in the usual manner. Eight days later, the animal's wound was healed and it apparently had recovered; after stimulation with histamine, free hydrochloric acid values of 60 units were noted with a pH of 1.61. A week later these values had fallen to 30 units of acid and a pH of 1.92. April 18, there was complete anacidity, which persisted until May 3 at which time one specimen revealed 20 units of free acid after stimulation with histamine. Greatly reduced values for free hydrochloric acid after both histamine and meat meals persisted until September 6. After stimulation with histamine on that date, free acid values of 65 units and a pH of 1.49 were found. On the following day, 3,000 *roentgens* were given over the intact upper portion of the abdomen. A week later there was little change in gastric secretion from the previous levels but, on September 21 and October 6, there was almost complete anacidity. October 13, 50 units of free hydrochloric acid and a pH of 1.58 were observed after stimulation with histamine. Approximately the same figures were obtained on October 27. A dose of 3,000 *roentgens* was administered November 2 and December 7, respectively. Neither of these doses produced any marked effect, although the quantities of gastric secretion obtained remained at a subnormal level and there was definite decrease of free acidity. February 28, the stomach was again exposed at laparotomy and 6,116 *roentgens* given over its anterior surface; lead shields to protect other viscera were used as before. Two weeks later the animal was in good condition, the surgical wound was partially healed, and there was practically complete anacidity after stimulation with histamine; a maximal pH of 2.45 was noted with 5 units of free acidity. During the entire period, the dog remained in satisfactory condition; a slight decline in weight was noted after each irradiation, but this was rapidly regained.

Dog 6: A bull terrior, weighing 11 kg., was prepared in the usual manner. May 23, 1933, 3,000 *roentgens* were administered over the surgically exposed stomach with the technic previously stated. For two months thereafter the gastric secretions were checked at frequent intervals and although some reduction in gastric acidity was noted, anacidity was not attained. August 8, 3,000 *roentgens* were given over the intact abdomen; eight days later the maximal gastric acidity after stimulation with histamine was 13 units and the pH 2.26. A week later gastric secretions were practically normal and they remained at or near this same level until November 6. On November 6, December 8, January 31, and February 28, respectively, this same dose (3,000 *roentgens*) was given over the intact upper portion of the abdomen. The dog remained in good condition, its weight was constant, no actinodermatitis developed, and gastric secretion, although persistently subnormal in acidity, was not abolished.

Dog 7: A male bull terrier, weighing 13.2 kg., was treated with 3,000 *roentgens* over its surgically exposed stomach on May 25, 1933, after the usual preliminary studies. The subsequent course of this animal, so far as gastric secretion was concerned, almost exactly paralleled that of dog 6. A temporary reduction of gastric acidity was noted, with subsequent recovery. On September 8, November 6, and December 8, 1933, and on January 31, 1934, respectively, 3,000 *roentgens* were given over the intact upper portion of the abdomen; gastric acidity was not greatly affected by any of these exposures, although there was a consistent 30 to 40 per cent reduction in the maximal levels of free acid after stimulation with histamine. The dog remained in good condition, except for the development of a small area of actinodermatitis in March, 1931.

Dog 8: A male terrier, weighing 13.3 kg., was used as a control. After the usual training period, 3,000 *roentgens* were given over the hind legs on June 2; September 11, November 7, December 11, 1933, and on February 1, 1934, respectively. Neither the gastric secretion nor the general condition of the animal was materially affected by this procedure.

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SINGLE GASTRIC POLYP*

REPORT OF AN INSTANCE

By

MARTIN G. VORHAUS, M.D.

and

ARTHUR E. T. ROGERS, M.D.

NEW YORK CITY, N. Y.

IN 1888, Menetrier[1] published a description of gastric polyp which stands as a classic in the interpretation of this condition. Since then, many reports have appeared so that, today, the subject is fairly well covered. An excellent review of the previous literature is incorporated in the thesis of Kirklin and Broders[2] of the Mayo Clinic. In addition to their review, four instances of solitary lesions of the stomach are cited in a group of nineteen cases of gastric polyposis.

Unquestionably, the most effective method of diagnosing polyp of the stomach is the roentgen study, provided proper technique is exhibited. All observers have emphasized the possibilities for error at roentgen observation dependent upon food residues in the stomach itself, pressure from the adjacent gas-laden colon, foreign bodies in the stomach, notably hair-balls, and gastric carcinoma of the polypoid type.

The following case report is published to emphasize, again, the necessity for accurate gastro-intestinal roentgen-studies in a patient where, clinically, the digestive disturbance was productive only of vague symptomatology.

CASE REPORT

R. C., female, age 50, admitted to the Medical Clinic complaining of generalized abdominal pains, occurring five to ten minutes after meals, radiating to the back and right shoulder and relieved by alkalis, accompained by distension, heart burn, belching, anorexia, loss of fourteen pounds in the past three months, and severe constipation.

Two years previously, a cholecystectomy had been performed at another institution for the above symptoms without relief. Additional facts in the past history include typhoid fever many years ago and a previous hysterectomy.

The physical examination revealed no pertinent findings except evidence of loss in weight. The laboratory study revealed normal findings for the urine and the blood; there was a low, normal gastric acidity value following food test meals.

Routine *gastro-intestinal X-ray studies* were made in this department. Stomach fluoroscopy and subsequent films disclosed a regular, constant, punched-out, filling-defect on the greater curvature of the pyloric antrum. On the opposite curvature, there was a fairly constant incisura. There was a considerable gastric residue seen by inspection of both the three- and six-hour progress films, each film exhibiting the greater curvature filling-defect. A diagnosis of single gastric polyp was made, dependent upon the character and persistence of the anomaly (Figs. 1 & 2 and 3 & 4).

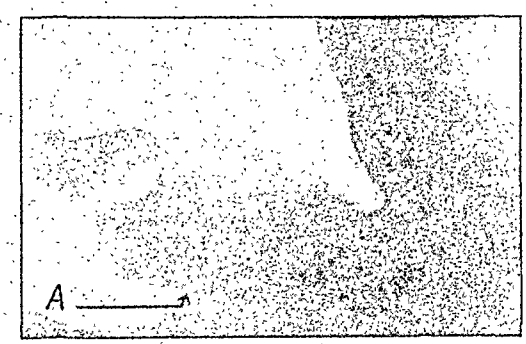


Fig. 1—Stomach immediately after ingestion of barium meal.

At operation, by Dr. Philip M. Grausman, a hard mass was felt about four inches from the pyloric end of the stomach. The stomach was opened and this mass was removed. The patient made an uneventful recovery.

Pathological examination, by Dr. Henry L. Jaffe, proved the specimen to be an inflammatory polyp of the gastric mucosa (Fig. 5).

Follow-up of the patient showed disappearance of symptoms previously noted pre-operatively.

DISCUSSION

Special interest in this case centers upon the vagueness of the symptoms which were associated with such relatively extensive pathology. Existence of upper abdominal pain, radiating to the back and right shoulder and accompanied by dyspeptic symptoms, had led to the incorrect diagnosis of



Fig. 2—Stomach immediately after ingestion of barium meal.

gall bladder-disease at another institution, on the basis of which cholecystectomy had been performed. No gastro-intestinal roentgenogram had been made at the first hospital experience and no report of the gall bladder studies which were made, is available. Unquestionably, prior to the first operation, gastro-intestinal roentgen films would have revealed the true nature of the pathological process in the stomach at that time as they did at our hands two years subsequently.

In gastric polyposis, occurrence of pain soon after meals is a frequent observation. The descriptions of the pain associated with gastric polyp vary as to its degree and location. Pain simulating biliary colic is, perhaps, one of the most infrequent types of all pain according to the various writers upon stomach polyposis.



Fig. 3—Stomach, three hours following barium meal.

The mechanism of pain production in our case is one which is open to conjecture. The roentgenograms demon-

*From the Department of Gastro-Intestinal Radiography, Hospital for Joint Diseases, New York City.

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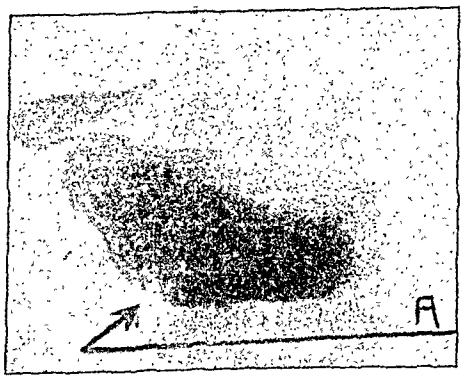


Fig. 4—Stomach, six hours following barium meal. Single gastric polyp—A.



Fig. 5—Photomicrogram of gastric polyp removed at operation.

strate clearly that the polyp was a considerable distance from the pyloric sphincter; its pedicle was so short that it could not have been displaced downwards sufficiently to produce pyloric obstruction. There may have been, of course, an associated pylorospasm but our films demonstrate no roentgen evidence that spasm existed. Antral spasm might have been associated with the lesion and is a possible cause for the pain, even though the pain's radiation and location are atypical.

At all events, these unusual types and locations of pain serve to emphasize the fact that pain resembling that of biliary colic in intensity, location and radiation may be due at times, to organic disease entirely extraneous to the biliary tract. The gastric polyp present in this patient was in a location and of a size readily demonstrable by routine gastro-intestinal X-ray examination. Even in the presence of clear-cut roentgen evidence of gall bladder pathology, it is sometimes advisable to study the gastro-intestinal tract; certainly, in those patients where, following cholecystectomy, the previous symptoms continue unabated, it becomes an absolute necessity that one rule out organic disease of the stomach as a cause. This case serves as an example: here one has a patient who was subjected to a totally unnecessary cholecystectomy and two years of additional post-operative suffering—a course which classified her as one of those patients unimproved by cholecystectomy—simply because no stomach roentgenograms had been made when distressing dyspepsia first arose.

SUMMARY

Report is made of an instance of single gastric polyp, accompanied by a clinical symptomology resembling biliary colic; of cholecystectomy followed by no benefit; the demonstration of the polyp, roentgenographically; complete disappearance of all digestive symptoms after surgical removal of the anomaly. Pathologically, the lesion was of inflammatory character.

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RECURRENT "HIATUS HERNIA" SYNDROME OF VON BERGMANN

By

FELIX CUNHA, M.D.*

SAN FRANCISCO, CALIFORNIA

RECENTLY, Hurst[1] described, under the title of this contribution, a peculiar type or variety of diaphragmatic hernia. He so named the anomaly because it had been brought to his attention at Von Bergmann's Clinic at the Charite in Berlin in 1931. Von Bergmann[2] stated that he regarded the disturbance of greater frequency than commonly was supposed and that it accounted for a large variety of sub-sternal symptoms for which no other adequate etiology could be designated.

Friedenwald[3] and his associates, in 1925, described this particular variety of hernia and first called attention to the fact that it was necessary to fluoroscope patients so affected in the recumbent position in order to demonstrate the lesion, since, in the upright position, it could not be seen. At the same time, these observers noted that forcible, deep inspiration during the examination, caused the hernia to become more prominent.

Hurst[1] believes that this particular variety of hernia should be separated from the more usual forms of hernia of the diaphragm commonly occurring through the oesophageal *hiatus*. He calls attention to its incidence being mainly in elderly persons and that the tissues immediately adjacent to the oesophagus as it passes through the diaphragm, are abnormally lax. This laxity Hurst attributes to senile atrophic changes with the consequent loss of tone. In the presence of such a point of lowered resistance, it is only necessary to add one other factor, namely, increased intra-gastric pressure, either intermittent or constant; then the same mechanical factors are present which produce herniae in other parts of the body.

Akerlund[4] described three types of *hialus herniae:*

a. *Congenital*—that associated with congenitally shortened oesophagus.
b. *Para-oesophageal*—where a portion of the lower oesophagus is in the abdomen and some portion of the cardiac end of the stomach bulges around that low-lying terminus.

*Instructor in Medicine, University of California Medical School, San Francisco. Visiting Physician, Gastro-Enterological Clinic, San Francisco Polyclinic and Post-Graduate Hospital.

Received for publication, April 5, 1934.

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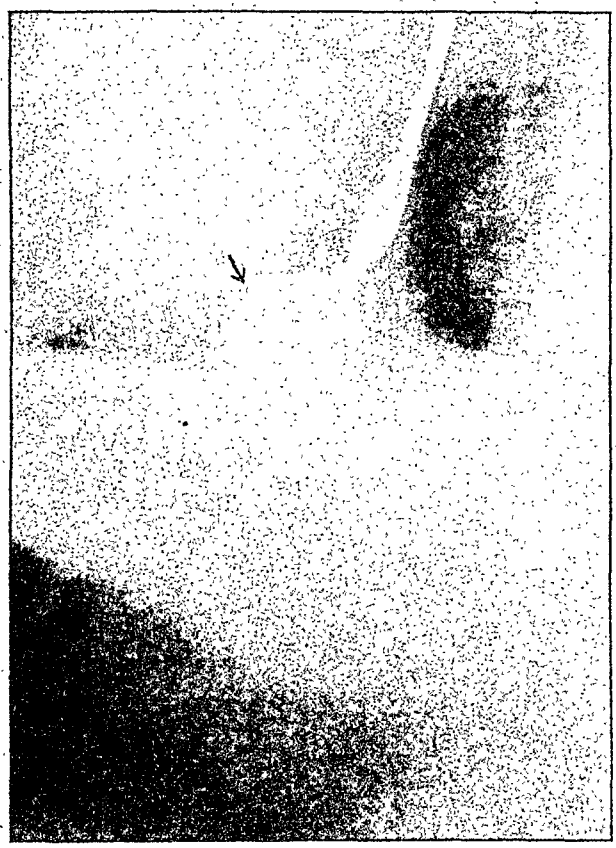


Fig. 1—Case 1—Radiogram taken with patient in extreme Trendelenberg position and using a thick barium mixture. In the upright position the "hiatus hernia" could not be visualized.

and later protrudes cephalad through the *hiatus oesophagi.*

c. *Hiatus herniae*—where there exists no congenitally shortened oesophagus.

Akerlund also gave as possible *etiological factors:*

a. *An embryonic defect*—a persistence of the *recessus pneumato-entericus.*

b. *Atrophy and lowered nutrition of the tissues*, with a consequent reduction in muscle tone.

The role of Auerbach's plexus in the hernia production also has been mentioned. Microscopically, degeneration of ganglion cells in the *plexus* accompanied by round-cell infiltration between the fibres has been described.

It is possible that faulty action of the cardiac sphincter itself may play a part or, there may occur disturbance in the innervation-mechanism, particularly of the sympathetic which is derived mainly from the cardiac plexus and the greater splanchnic nerves.

Observation of Case 1, cited below, brought out that, symptomatically, the patient was much worse when in periods of emotional stress.

SYMPTOMATOLOGY

Clinically, the complaint may resemble either ulcer or gall bladder disease. Most prominent, however, usually is *substernal distress or pressure:* this may be anginoid in type and be referred to the left shoulder and down the arm. *Dysphagia* may be experienced, but, in our two cases, the complaint was of food passing up and down the oesophagus and seemingly not getting into the stomach.

Usually, *pain* is present and of varying degree of severity. Often it is sub-sternal or is sharply localized in the mid-epigastrium or referred through to the back in the region of the 7th or 8th dorsal costo-vertebral junction. Sub-sternal pain was present in both the patients to be described. *Nocturnal distress* and aggravation of all symptoms, particularly the increase in sub-sternal pressure, present when lying in bed and relieved upon sitting erect, frequently is encountered. Regurgitation of food or actual vomiting may be noted.

Inflammation of the involved area is possible; it occurs secondary to irritant substances in the diet. These may produce first, abrasions and, subsequently, if the irritant continues, actual inflammation.

Ulcer of the lower end of the oesophagus is not particularly uncommon; such may easily occur in an area of lowered nutrition and lack of *tonus.* In such event, the symptoms may be those common to ulcer; occult blood in the stools may be an accompaniment.

Roentgenological Aspects: It is perhaps most important to bear in mind that this particular type of hernia cannot be visualized in the upright position; often it is necessary to place the patient in recumbent positions, varying the angles of vision during the study, in order to demonstrate the lesion. This is well illustrated by Case 1, below; it was necessary to place the patient in the extreme Trendelenburg position and to use a very thick barium mixture before a satisfactory result was obtained.

A second important fact is that the condition may be intermittent in the character, the degree of its manifestations subject to psychic or emotional influences. At times, the hernia actually may be not present. Thus, repeated examinations are required to demonstrate it. This peculiarity may account for failure to discover the hernia in several early roentgen examinations in Case 1, particularly when taken in association with this patient's aggravation of symptoms when under emotional stress, a fact which was not discovered for some time.

Deep-breathing manoeuvre: The effect of having the patient carry on forced deep inspiration to aid in visualization of the hernia, is not to be minimized; it is a distinct help.

The constancy of visualization is dependent upon several factors:

a. Size of the hernia—usually it is about as large as a walnut.
b. The size of the oesophageal orifice.
c. The amount of muscular contraction around the oesophageal opening.
d. The position of the patient.
e. The influence upon the hernia of forced, deep inspiration, particularly with regard to making it more prominent.
f. Special roentgen technic, position of patient, etc.

TREATMENT

Hurst has summarized the treatment of the condition as being directed mainly toward the avoidance of increase in intra-abdominal, and hence, sub-diaphragmatic pressure.

Flatulency and increased sub-diaphragmatic pressure caused by carbohydrate fermentation in either the stomach or the intestine must be controlled by diet and, occasionally by the use of such preparations as diastase or charcoal. Colloidal kaolin was administered in our Case 1, with beneficial result.

Avoidance of any constricting belt or tight garments about the abdomen.

Elimination of roughage and bulk from the diet; bland smooth diet is preferable. With some patients, small meals at rather frequent intervals, say 2-3 hours, appear to lessen lower oesophageal irritation.

Relief of the nocturnal, sub-sternal distress if present, can be accomplished to some extent by having the patient sleep with head and shoulders elevated so that any increased intra-gastric pressure is not directed upward against the diaphragm.

If there is reason to suspect that true inflammation is present or that actual ulceration had taken place, supplementing the smooth diet with anti-spasmodics, as belladonna, papaverine, etc., may hasten favorable outcome, by relaxation of the cardiac-sphincter spasm. Alkaline therapy, as in



Fig. 2—Case 2—Roentgenogram taken with patient in recumbent position. In the upright position the "hiatus hernia" not visualized.

instances of peptic ulcer, generally is indicated, where concomitant with the hernia ulcer is proved or suspected.

CONCLUSIONS

1. This syndrome probably is more frequent than has been considered; in cases where digestive symptoms predominantly are sub-sternal and no satisfactory explanation can be found, this area should be subject to close scrutiny in order to prove the presence or absence of "hiatus hernia."

2. The diagnosis is best made by fluoroscopic examination and then confirmed by X-ray films. Since the lesion may not be visible with the patient upright, observations of the patient in the recumbent or the Trendelenburg position are necessary in order fully to demonstrate or to exclude the anomaly.

3. A careful clinical history eliciting the type of substernal distress, the sensation of food moving up and down in the oesophagus plus the tendency for nocturnal aggravation of symptoms, oftentimes will suggest the diagnosis and lead to carrying out of technical procedures which reveal the lesion.

The two cases cited here were seen recently in the course of complete gastro-intestinal studies:

CASE HISTORIES

CASE 1.—Male. Age 69. Retired. Complained of pain, described as boring in character, localized just to the left of the ensiform and which radiated through to the back at the level of the 8th costo-vertebral junction. Pain has been present for varying intervals for past five years but, whereas formerly, it was mild and occurred at varying intervals, now it is constant and more severe. He has noted that the pain is relieved when his stomach is empty and seems to be increased on taking food. No nausea, but the patient vomits quite frequently usually *almost immediately after eating*, vomitus usually consisting of digested food particles. He has noticed that his symptoms seem to be increased at night and he has been unable to get to sleep satisfactorily; may awake with pain and a pressure under the sternum which is relieved by walking around and drinking hot water. Has awakened every hour during night for past two months. Has lost 20 lbs. since symptoms became severe but he attributes this to not eating in order to avoid pain. Before the pain became constant and severe he noted that a large meal or taking a large quantity of fluid would bring on pain. He has had considerable financial and family worries and has noticed that when he is more disturbed mentally his symptoms are much worse.

Complete Roentgen studies have been made several times during the past five years by various physicians but have always been reported negative. He has experienced prolonged medical ulcer-regimes but with indifferent results.

Patient stated that, at a previous examination, an attempt had been made to pass a stomach tube but that he had bled so profusely that the tubing had been abandoned. About three months later another unsuccessful attempt resulted in profuse hemorrhage.

After examining the cardio-cosophageal region in the upright position, the patient was placed in the recumbent position but no abnormality was noted, but when he was placed in the extreme Trendelenburg position and swallowed a very thick, barium mixture, a hernia about the size of a small walnut could be demonstrated. (Figure 1). Placing the patient again in the upright position the barium passed into the stomach and the lesion could not be seen. An oesophagoscope was passed for the entire length of the oesophagus, but no abnormality was noted. During the examination there was no bleeding and no apparent cause discovered for the previous profuse hemorrhages when stomach tubes were passed. (Figure 1).

CASE 2.—Female, widow, age 40 years. *Complaint:* Substernal pain and distress for past year, usually occurring immediately after meals and accompanied by a sensation of food sticking half way between pharynx and stomach. Pain is mild, described as a dull, constant ache sharply localized in one spot. No nausea or vomiting, some belching of gas and regurgitation of food. Bowels move normally, no dark colored or tarry stools observed. At night on retiring, the pain and pressure are worse and the patient obtains relief by drinking several glasses of hot water; otherwise the distress will keep her awake for hours. No loss in weight, although during the past two months symptoms have increased markedly in severity, particularly the localized pain; she has placed herself upon a milk and egg regime with slight relief.

Roentgen Examination: Fluoroscopically, in the upright position oesophagus and stomach entirely negative. Placing the patient in the Trendelenburg position, a small hernia the size of an almond was seen in the lowest portion of the oesophagus just above the diaphragm. (Figure 2).

ABSTRACTS

PRATT, JOSEPH H.
"A Study of Steatorrhea, with special reference to its occurrence in Pancreatic Disease and Sprue." Am. Jour. Med. Sc., Vol. 187, No. 2:222, February, 1934.

The author points out that serious errors are made in attempting to determine the amount of fat present in the feces by gross and microscopic examination, and that the recognition of most cases requires the careful and time consuming methods of the chemist. It is essential that the exact amount of ingested fat be known. Adolph Schmidt's standard diet is recommended. A knowledge of the percentage and amount of fat absorbed from the food is of far greater value than the determination alone of the percentage of fat in the feces.

The fat content of the dried feces was determined in thirty-three cases. The utilization of starch in the food was normal in all the cases of steatorrhea studied. The determination of the percentage of nitrogen in the feces has proved of no value in diagnosis. Most of the cases proved to be sprue or pancreatic disease.

Comment: It is gratifying to know that high-grade chemical feces work is being carried on in these days of rapid Roentgen-ray diagnosis of abdominal disease. In one of the writer's cases, a diagnosis of steatorrhea was made, due to pancreatic disease. The patient had had a gastro-enterostomy performed some months previous to the establishment of this diagnosis. The autopsy revealed that the surgeon had inadvertently attached the terminal ileum to the stomach.

H. W. Soper.

HURST, A. (London).
Stomach Diseases as Entities. Archives f. Verdauungskrankheiten, January, 1934, Vol. 55, No. 1-2.

Hyper and hyposthenic gastric constitutions are associated with hyper and hypochlorhydria, respectively. These types may become more susceptible to gastritic insults either because of lack of HCl or because of lack of the protective mucoid secretion as the result of a too rapid emptying of the stomach. Gastritis reduces the HCl content of the stomach rendering in some cases hypochlorhydric types into complete achylias. Secondary effects of gastritis: in hyperstenic individuals it is more prone to cause ulcers or ulcerous gastritis due to the effect of HCl on denuded areas. In hyposthenic persons the association with achlorhydria is not uncommon, leading often to a gastro-enteritis. The latter predisposes to various infections (lack of destruction of organisms), or even toxic allergic conditions (rheumatism, rosacea). Relationship with pernicious anemia is stressed, while that of a simple anemia is also mentioned. Cancer of stomach: about 65 per cent of the cancers develop from chronic gastritis, the remaining ones are superimposed on gastric ulcers. Hypersthenic types never develop pernicious anemia although they may be afflicted with ulceration. Hyposthenic types on the other hand are frequently the victims of pernicious anemia without ulceration. Both types, however, are liable of carcinomatous degeneration.

M. E. Gabor.

KOGAN, D. A.
The Differential Diagnosis of Pylorostenosis and Pylorospasms. Archives f. Verdauungskrankheiten, January, 1934, Vol. 55, No. 1-2.

There are not positive criteria to differentiate these two syndromes with the usual methods. The presence of lactic acid is also not pathognomonic for stenosis produced by cancer. The author advises strychnine injection (1:1000 and up) which promotes peristalsis. In cases of spasms a re-establishment of the normal flow is attained while the true stenotic stomachs suffer an exacerbation of vomiting produced by antiperistalsis. He suggests the same agents in oesophageal spasms and stenoses.

M. E. Gabor.

PALMER, WALTER LINCOLN AND HEINZ, THEODORE E.
"Mechanism of Pain in Gastric and Duodenal Ulcer"—Study vii: Further Observation, Arch. Int. Med. 53:269-285, 1934.

In this article a survey of the literature relative to ulcer pain has been made. Experimental work by the authors on patients with benign gastric ulcer, duodenal ulcer and gastric carcinoma is presented, including observations of the acidity during spontaneous distress, the production of ulcer pain with physiologic solution of hydrochloric acid, and by subsequent stimulation with histamine hydrochloride, Kymographic and roentgenologic studies of the stomach during distress, together with the effect of calcium chloride and atrophine sulphate on ulcer pain.

The studies suggest a relationship of gastric acidity to ulcer pain; that ulcer pain ordinarily is independent of gastric peristalsis, gastric tone, intragastric pressure and pylorospasm, except as these influence gastric emptying, thereby affecting the chemical nature of the fluid bathing the ulcer. Atropine sulphate intravenously did not desensitize the pain producing mechanism, while calcium chloride by intravenous route temporarily afforded relief. The acid acting directly on exposed nerve endings in an irritable tissue is defined as an adequate stimulus for the production of pain. (*Comment:* No tissue sections are exhibited to prove that such "exposed nerve endings" actually exist and apparantly no control studies have been made on animals in which the nerve pathways have been "blocked" in order to check up pain responses when acid action upon "exposed nerve endings" has been made impossible.)

E. B. Freeman.

WILE, UDO J., M.D., AND SAMS, WILEY M., M.D.
A Study of Jaundice in Syphilis. Its Relation to Therapy. Am. Jour. Med. Sciences, March, 1934.

Jaundice in early syphilis has been reported since the 16th Century and its appearance with late syphilis, especially cirrhosis, is not uncommon. This study was made under four headings, viz: (a) Untreated cases of jaundice and syphilis; (b) jaundice following treatment for syphilis with one of the arsphenamines; (c) infectious jaundice; (d) syphilitics who develop jaundice during or after malarial therapy.

10,021 cases of syphilis were seen in the University Hospital (Ann Arbor) from January 1, 1925, to March 1, 1933, and the incidence of jaundice before treatment was 0.18 per cent (18 in 10,021 cases). Of these cases 4126 were treated with one of the arsphenamines and 56 developed jaundice (1.35 per cent). This is 7.5 times as frequent as pretherapeutic jaundice. Cases of post-arsphenamine jaundice can be separated into early and late types. In early cases jaundice appears in from 1 to 15 days and may be ascribed to Herxheimer reactions or toxic reactions.

Late post-arsphenamine jaundice occurs, on the average, 80 days after the last intravenous treatment. There are three major theories as to the cause of the late icterus: (1) delayed toxic action of arsphenamine on the liver; (2) a hepato-recurrence; and (3) an intercurrent infection usually in the nature of a so-called "catarrhal jaundice."

Arsenic jaundice is much more frequent than jaundice in the population as a whole. Ruge found it to occur 16 times more frequently among the personnel of the German Navy treated with salvarsan than among the rest of the Navy. After recovery patients may again tolerate arsphenamine without a return of jaundice. The authors' experience and arguments do not altogether agree with the contention of Milian that 90 per cent of late cases of jaundice result from a recurrence of syphilis in the liver (hepatorecurrence).

Under number 9 of the conclusions the authors state: "Until more accurate means are at hand to determine susceptibility and liver function, and until the drug is modified to make it less hepatotoxic, post-arsphenamine icterus will continue to be among the severe complications of the modern treatment of syphilis."

Allen Jones.

MORRISON, THEODORE H., M.D., F.A.C.P., AND FELDMAN, MAURICE, M.D., BALTIMORE, MD.
The Redundant Duodenum: Clinical Significance. Annals of Int. Med., 7, 9, March, 1934, 1126.

Instead of the usual C shape of the duodenum it may assume a U shape or V shape or other abnormal pictures.

Normally the first portion of the duodenum is somewhat mobile, the remaining portions less so.

The looping in the redundant duodenum is caused by an anomalous condition of the hepato-duodeno-colic ligament. Ptosis of the superior portion of the duodenum results in a loop in which there occurs a delay in the passage of the opaque meal. There is a marked elongation or lengthening of the superior segment of the duodenum in cases of redundancy.

The term dolichoduodenum is preferred to "the redundant duodenum."

Radiographic pictures show a loop like a diverticulum in the duodenum just beyond the cap. The symptoms, while not characteristic, usually include anorexia, nausea, epigastric discomfort, vomiting and headache; so-called bilious attacks may have occurred for years. Duodenal stasis is usually present. With frequent attacks, loss of weight and strength and neurasthenic symptoms may develop. Constipation in some, diarrhoea in others, may be present. Mild pain may be noted. Hepatic enlargement and tenderness under the right costal arch may supervene. Gastric secretion is variable; hyperchlorhydria being found in a small majority.

Accurate diagnosis of the condition depends upon X-ray demonstration. In the authors' cases peptic ulcer was frequently found and gallbladder infection rarely so.

In the diagnosis repeated Roentgen-ray examinations should be resorted to in order that the permanency of the condition may be established.

In the treatment of the condition a bland diet of high caloric value, rest in bed for four to six weeks with the foot of the bed elevated, especially in those cases associated with marked enteroptosis, ulcer and the more severe grades of duodenal stasis. Surgical measures, duodeno-duodenostomy, duodeno-jejunostomy or gastro-jejunostomy may be resorted to.

Operation was not performed in any of the authors' cases.

The Abstractor considers this an important subject and the contribution valuable and timely.

Allen Jones.

SECTION II—*Experimental Physiology*

AN INVESTIGATION CONCERNING CERTAIN SUBSTANCES REPORTED TO AFFECT THE MOTILITY OF THE GALL BLADDER*

By

W. L. VOEGTLIN *and* A. C. IVY

CHICAGO, ILLINOIS

RELATIVELY few observations have been published regarding the pharmacology of the gall bladder *in situ* in the dog, although much work has been done on strips of the gall bladder and on the isolated gall bladder. The results of many investigators regarding the effects of certain drugs on the motility of the isolated gall bladder are not in agreement, except when the more potent drugs were used. The results on the effects of drugs on the gall bladder *in situ* are also in conflict. These conflicting reports probably are due mainly to the inadequate control of extrinsic factors which play a role in the evacuation of the gall bladder as well as to the employment of inadequate methods of recording changes in intravesicle pressure. Those factors, which, aside from the physiological state and response of the intrinsic musculature, may cause an apparent contraction or relaxation of the gall bladder are: (a) changes in liver volume, (b) increased gastric or duodenal motility, (c) changes in intra-abdominal pressure, (d) increase or decrease in the muscular tone of the abdominal muscles or of the diaphragm and (e) variation in the depth of anesthesia.

In the present study, these factors have been eliminated or controlled, and the effects of certain drugs on the motility of the gall bladder *in situ* in the dog has been determined, utilizing a sensitive method for the determination of changes in the intravesical pressure.

METHODS

Changes in the intravesical pressure were recorded by the method of Ivy and Oldberg (17) which was found to record slight changes satisfactorily. The cystic duct was clamped, avoiding the cystic artery, and a trocar was placed in the dome of the gall bladder. Recordings were made by connecting the trocar to a Beckmann tambour writing on a smoked drum. Changes in liver volume, intestinal motility and muscular tone of the abdominal muscles and diaphragm were controlled, in the case of those drugs causing apparent contractions or relaxations of the gall bladder, by inserting a rubber balloon between the lobes of the liver. This balloon was in turn connected to a second tambour after the method of Bainbridge and Dale (2.) Any changes recorded by the gall bladder tambour which were duplicated by the tambour connected to the phantom gall bladder were rejected as being the result of extraneous factors. Changes in intra-abdominal pressure were eliminated by allowing the abdominal incision to gape and covering it with a towel. Narcosis was maintained at a constant level by running the experiments under barbital, using ether only during the operative procedure. Since *cholecystokinin* is the most potent excitor of the gall bladder known at the present time, all gall bladders were tested by preliminary injections of this material. Only those responding satisfactorily to this stimulus were used in investigating the following substances: *pilocarpine, calcium chloride, pituitrin, choline (acetylcholine), methyl guanadine, hydrochloric acid, hypertonic sodium chloride solution, cystine, papaverine, atropine, epinephrine, ephedrine, peptone, magnesium sulphate,* and *various fatty substances.* These substances were injected intravenously, while solutions of *peptone, glucose* and *magnesium sulphate* also were administered by transduodenal instillation. The dogs were fasted 24 hours prior to the experiment to insure well filled gall bladders.

RESULTS

Pilocarpine is said to cause a contraction of the gall bladder *in situ* in dogs or isolated (18) (30) (34) (35) and in the cat (26). Little or no evacuation of the visualized gall bladder under the influence of pilocarpine, however, has been demonstrated in man (14) (20) (27), or in dogs or cats (3) (32). In our experiments, pilocarpine in doses of 1/2 mgm., *in toto*, gave a strong, well sustained, tonic contraction of the gall bladder *in situ* in each of four barbitalized dogs. Changes in liver volume, as recorded by the phantom gall bladder, occurred with the fall in blood pressure, but persisted for a shorter period than the changes in intravesical pressure. The contraction of the gall bladder was promptly relaxed by atropine.

In four dogs, the gall bladder was visualized with *tetraiodophenolphthalein.* No diminution in the size of the cholecystogram was noted in any of these unanesthetized dogs after the subcutaneous injection of 4 mgm. of pilocarpine. The gall bladder bile might be moved into the cystic duct, but no discharge into the duodenum followed. Since we know that pilocarpine markedly increases the resistance offered by the intramural portion of the common bile duct to the flow of bile into the duodenum, these results are not surprising. In other words, pilocarpine produces a biliary dyskinesia. These results confirm those of Bassin and Whitaker (3) on the dog and the cat, and the observation that pilocarpine is not effective in causing gall bladder evacuation in man (*vide supra*).

Pituitrin. This substance according to some reports either relaxes or has no effect on the gall bladder *in situ*, or isolated, of dogs and guinea pigs (5) (13). Kalk (19) reports an immediate primary relaxation with a secondary rise in gall bladder tone in decerebrate cats after a latent period of 5-15 minutes following the intravenous administration of pituitrin. Similar changes in the human gall bladder have been demonstrated roentgenographically. Many investigators have reported on the evacuation of the gall bladder in man following the subcutaneous injection of 1 or 2 cc. of pituitrin (3) (4) (14) (19) (20) (27) (33) (et al).

In our experiments, "*pitressin*" (the pressor—diuretic-antidiuretic fraction of pituitary extract) when given intravenously in doses of 1 cc. caused a strong rise in intravesical pressure in six dogs and slight relaxation in one dog. The rise in pressure followed a latent period of from 10 to 18 minutes during which period the gall bladder often showed an apparent relaxation. Since this fall in pressure did not invariably occur, and when it did occur it was accompanied by a decrease in liver volume, we believe the pressure fall to be an artefact insofar as the gall bladder is concerned. The height of the contraction is attained in from 1 to 2 hours after injection and is considerable, corresponding to as much as 15 cm. of bile pressure, pitressin, when administered subcutaneously in doses of 2 to 4 cc., gave variable results. A rise

*From the Department of Physiology and Pharmacology, Northwestern University, Chicago.

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in gall bladder pressure occurred in 4 dogs, while relaxation was seen in one dog. No apparent effect was noted in 2 dogs. The latent-period following the subcutaneous injection of pitressin was about 45 minutes with the smaller doses (2 cc.), although only a very short latent-period (4-6 minutes) followed the administration of 4 cc. The maximum rise in intravesical pressure was 10 cm. of bile pressure. The oxytocic principle of pituitrin ("*oxylocin*," Parke Davis and Co.) was irregular in its action. A small contraction was seen in 3 dogs, relaxation in two and no apparent effects in two, when this substance was injected, intravenously, in amounts of 1 cc. A transient fall in blood pressure accompanied each of the injections. In those trials which revealed a contraction of the gall bladder, no appreciable latent-period preceded the rise in intravesical pressure. The rise quickly reached a maximum (2-4 cm. bile pressure) and slowly subsided in about 15-20 minutes.

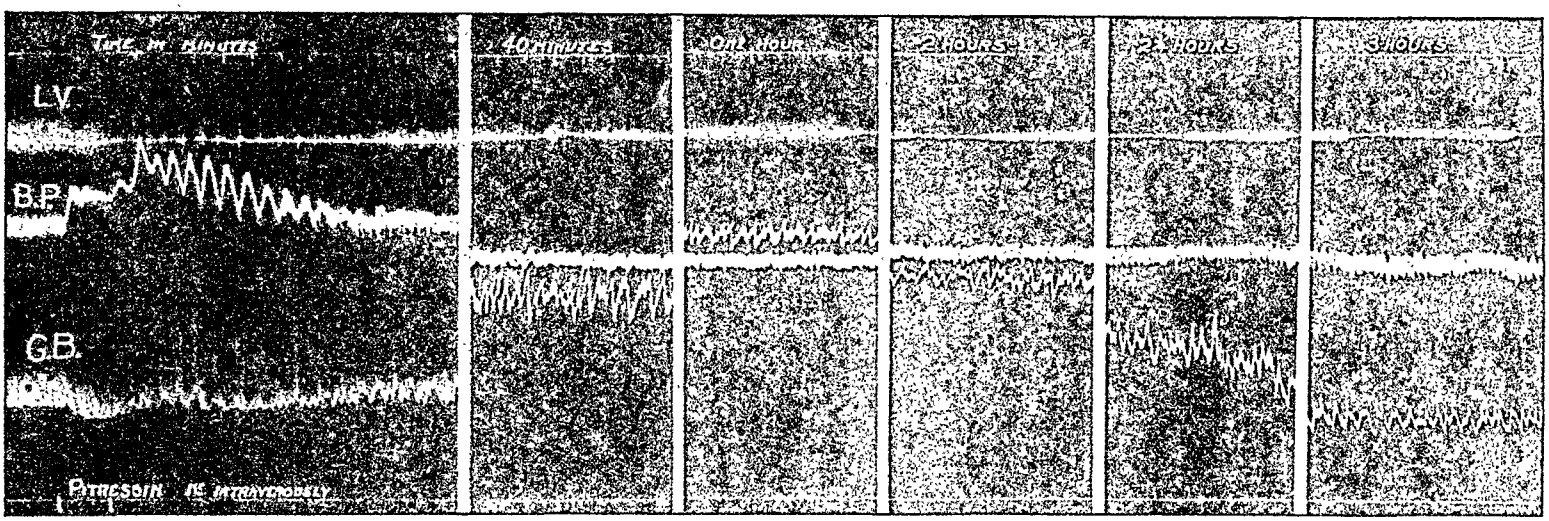
Our results with pitressin in the dog with the gall bladder *in situ* were similar to those of Kalk (19) on the human gall bladder when studied roentgenographically and in the decerebrate cat. Our observations, however, contradict the findings of Houssay and Rubio (15), who used the transplanted gall bladder, in the dog. It is possible, in view of the thought to be produced by factors other than a true muscular contraction of the vesicle.

Hydrochloric acid. Three to 10 cc. of N/20 HCl when injected intravenously were found to have no effect on the motility of the gall bladder *in situ* in dogs. This experiment was performed primarily to ascertain if the absorption in the intestine of the HCl of the gastric juice might have an effect on the gall bladder.

Sodium chloride solution. Hypertonic sodium chloride solution which is known to increase the propulsive motility of the intestine when injected intravenously (30%), has been reported to have an inconstant effect on the gall bladder in dogs (29) (31). This substance when injected intravenously in amounts up to 20 cc. failed to give a motor response in four dogs.

Cystine. Cystine HCl in amounts up to 5 cc. of a 0.2% solution gave no rise in intravesical pressure. Cystine was used because preliminary tests indicate that it is present in cholecystokinin.

Papaverine. This drug has been said to cause relaxation of gall bladder strips from the dog and the cat (24) and of the isolated gall bladder of the guinea pig (10) (11). In our experience this drug caused no decrease in the intravesical



Record on smoked drum of gall bladder contractions following injection of Pitressin.

long latent-period, that these workers did not observe their preparations sufficiently long to note the delayed contraction. We have no explanation to offer regarding this delayed contraction of the gall bladder after pituitrin, which is a very interesting phenomenon when compared with the action of cholecystokinin and pilocarpine.

Calcium chloride intravenously has been reported as causing some evacuation of the gall bladder (3) (4). No rise in intravesical pressure was noted in any of our five dogs injected with a 5% solution of this salt in amounts up to 5 cc., although some augmentation of the tonus rhythm was regularly observed.

Choline (acetylcholine) may cause some slight evacuation of the gall bladder in man (14) and in the cat (4). When this drug is injected, a marked change in liver volume occurs along with the fall in blood pressure, but a true contraction of the gall bladder *in situ* was not noted in any of the three dogs following the intravenous injection of this substance. If a contraction of the gall bladder *in situ* occurs in the dog, it is entirely masked by the effect of the change in liver volume incident to the fall in blood pressure.

Guanadine (methyl guanadine sulphate) is said to be without effect on the isolated gall bladder of the guinea pig (10). In doses of 2 mgm. per kilogram it caused a brief rise in intravesical pressure in two dogs in our series. This rise was coincidental with the rise in blood pressure and was duplicated by the phantom gall bladder. It was therefore

pressure upon the intravenous administration of 15 mgm. or the subcutaneous injection of 25 mgm., either during the resting stage, or at the height of a tonic cholecystokinin contraction. If papaverine is effective in relieving biliary colic, its action must be on other tissues than the gall bladder. However, it does not cause an increase in the tonus rhythm of the gall bladder as morphine generally does.

Novocaine. This drug has been reported to relax the isolated gall bladder of the guinea pig (10) (11). Infiltration of the abdominal incision with 20 cc. of 2% procaine caused no relaxation of the viscus in either of our two dogs within one hour.

Atropine is said to cause relaxation of the gall bladder of the guinea pig, dog, cat, and monkey when isolated and *in situ* (2) (5) (6) (7) (8) (16) (22) (35) et al. We found that atropine promptly relaxed the contraction induced by pilocarpine. Only occasionally it relaxed slightly the resting gall bladder. Neither did it abolish the response of the gall bladder to cholecystokinin, but it may decrease the vigor of the response. Atropine is the most potent drug, except deep ether anesthesia, which we have tried for decreasing gall bladder tone.

Epinephrine. This agent is variously reported as causing contraction, relaxation, or as having no effect upon the gall bladder when isolated or *in situ* (2) (5) (8) (13) (21) (*et al*). We were unable to demonstrate any constant effect following the intravenous injection of even as much as 1 cc. of 1:1000

solution, slowly. A slight relaxation was observed in two dogs following this dose which, given intravenously, is enormous.

Ephedrine. This drug, which in many instances acts like epinephrine, but more slowly over a more prolonged period, had no effect on the gall bladder motility. Doses of 20-25 mgm. were administered intravenously. In this dose blood pressure is markedly elevated (40-100 mm. Hg.).

Peptone (Witte). This substance was administered intravenously in a 1% solution in amounts up to 5 cc. An irregular rise in intravesical pressure coincidental with blood pressure changes resulted. The rise in intravesical pressure was duplicated by the tracing from the artificial gall bladder, showing that the rise in intravesical pressure was *not due to a true contraction* of the gall bladder. The trichloracetic acid precipitate from 3 grams of Witte's peptone, when injected intravenously, produced only a slight vasodepressor effect and no effect on gall bladder motility. The trichloracetic acid precipitate was used because this reagent precipitates cholecystokinin from peptone-containing solutions.

Similar results were obtained when a peptone from another source (Armour) was used. Thus it is evident from these results, that when peptone is instilled into the duodenum to effect gall bladder evacuation, it does not act specifically on the gall bladder after absorption into the blood.

Fatty substances. Various fatty substances were injected intravenously without obtaining any contraction of the gall bladder. These included the *non-saponifiable fraction* from 200 cc. of olive oil, glycerol (3 cc.), and oleic acid (5 cc.). The intravenous injection of chyle (120 cc. containing 1.0-2.5% fat) collected from the thoracic duct of dogs which had been fed a fat meal (egg yolk and cream) was ineffective in causing a contraction of the gall bladder *in situ*, in barbitalized dogs. Neither did it cause any decrease in the size of the cholecystogram in any of three unanesthetized dogs. The mechanism of the apparent contraction of the gall bladder following the intravenous injection of oil emulsions and the effect of various digests of fat has been reported in another publication (31). Thus, we have so far been unable to demonstrate that an agent present in food or resulting from the digestion of food causes gall bladder contraction upon being administered intravenously.

Magnesium sulphate. This substance when injected intravenously has been reported to depress slightly the gall bladder of the dog *in situ* (23). In our experiments, this substance on intravenous injection (200-300 mgm.) was without effect on the gall bladder response to cholecystokinin.

Magnesium sulphate. Solutions of magnesium sulphate (25-33%) when placed in the duodenum of anesthetized dogs have been reported to cause evacuation of the gall bladder (25) (28). Others have been unsuccessful in confirming this (1) (9) (12). In our experiments the duodenal instillation of 33% magnesium sulphate in amounts up to 70 cc. showed conflicting results. One dog showed a slight, but definite increase in the tonus rhythm of the gall bladder; another manifested slight relaxation; and six other experiments were entirely negative.

In these experiments it is to be recalled that the *nerve paths were blocked*, at least most of them. We were primarily interested in ascertaining if magnesium sulphate acting in the intestine effects evacuation of the gall bladder *by producing the hormone cholecystokinin*, and not in attempting to obtain a reflex contraction. In answer to this question our results show that if magnesium sulphate acting in the intestine does excite cholecystokinin production, the action is feeble and variable, considerably more feeble and variable than when dilute hydrochloric acid or "fatty digests" are present in the upper intestine. We believe that magnesium sulphate effects evacuation of the gall bladder primarily by decreasing the intramural resistance of the common bile-duct. That a reciprocal nervous mechanism is concerned in magnesium sulphate "evacuation" has yet to be demonstrated. (For a review of the literature, see Reference 16a).

Peptone. Peptone, by duodenal instillation, has been widely used in human patients as a means of evacuating the gall bladder. Attempts to show a contraction of the gall bladder *in situ* in anesthetized dogs following this procedure have been negative (1). We were also unsuccessful in demonstrating any rise in intravesical pressure after the introduction of 200 cc. of Witte's peptone into the duodenum of barbitalized dogs. The results cited above on the effect of peptone intravenously on the gall bladder show that peptone does not act by being absorbed into the blood unchanged. The mechanism by which peptone instilled into the duodenum causes more or less evacuation of the gall bladder, we believe is analogous to that of magnesium sulphate.

Glucose. From 60 to 75 cc. of 60% solution of glucose, when placed in the duodenum of barbitalized dogs, was ineffective in causing any change in gall bladder tone over a period of 30 minutes. Hypertonic glucose was used because some investigators (35) have used it in man to produce evacuation of the gall bladder. If it causes evacuation of the gall bladder, it must act similarly to magnesium sulphate.

CONCLUSIONS

1. Cholecystokinin, pituitrin and pilocarpine are the only drugs which we have investigated which, when injected intravenously into barbitalized dogs, give what we interpret to be a true, muscular contraction of the gall bladder *in situ*. (It has been shown by others that ergotamine may increase the tone of the gall bladder *in situ* (2) (5) (23).)

2. Pituitrin. This drug is particularly interesting in that it causes a slow, gradually increasing contraction of the gall bladder of the dog which appears *only after a latent period* of from 10 to 18 minutes, whereas cholecystokinin and pilocarpine *cause a contraction within a minute* after intravenous injection. (This action of pituitrin on the dog's gall bladder is the same as that reported for the human gall bladder by Kalk.)

3. Cholecystokinin is the only substance known that causes gall bladder contraction on intravenous injection in the dog without a concomitant change in blood pressure or a general parasympathetic stimulation.

4. Calcium chloride regularly increases the tonus rhythm of the gall bladder of barbitalized dogs when injected intravenously.

5. Methyl guanadine, choline, hydrochloric acid, hypertonic solutions of sodium chloride, cystine, various fatty substances, papaverine, epinephrine, ephedrine, magnesium sulphate and peptone upon intravenous injection have no direct effect on the motility of the gall bladder *in situ* in barbitalized dogs.

6. Atropine appears at present to be the most reliable drug to produce relaxation of the gall bladder, although it is not marked in its action, and does not prevent the action of cholecystokinin, but does prevent the action of pilocarpine.

7. The intraduodenal instillation of magnesium sulphate, peptone and glucose does not lead to gall bladder contraction and evacuation *via a humoral or hormone mechanism.* If magnesium sulphate when administered intraduodenally does cause the formation of cholecystokinin, the amount formed is meager in comparison with that formed when dilute acids and "fatty digests" are introduced into the duodenum.

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THE ANTIPEPTIC INFLUENCE OF GASTRIC MUCIN*

By
EARL A. ZAUS, M.D., *and* LEONARD S. FOSDICK, PH.D.
CHICAGO, ILLINOIS

COMMERCIAL gastric "*mucin*" is offered as a physiologic substance or method to promote the healing of peptic ulcers.[1] [2] Like other agents used in ulcer therapy, it is supposed to protect the regenerative response against the action of the digestive juice. *The mechanism of its action is considered threefold:* 1. reduction of the free acid; 2. mechanical protection; 3. inhibition of peptic activity.

In vitro experiments have shown that one gram of commercial *mucin* "combines" with 12 to 15 cc. of a 0.1N/HCl solution†[3], about one-tenth the amount which a similar quantity of $NaHCO_3$ is capable of neutralizing. Therapeutic doses, for the control of the free acid, are calculated upon this basis. Clinically, however, these doses have not uniformly proven effective in the control of gastric acidity[4] [5].

Endogenous mucus probably is a major agent in the protection against mechanical and chemical irritants. Thousands of mucus cells pour their secretion upon the surface. The mucus, which is known to resist peptic digestion, adheres firmly to the surface-epithelium and gastric "pits." It is more difficult to get experimental evidence to show that, orally administered, *mucin* supplies the same kind of mechanical protection than it is to find clinical proof of such action. Clinical workers have seen patients in whom alkali management had failed to arrest symptoms in whom the substitution of *mucin* has resulted in the prompt relief of symptoms.

Laboratory experiments,[1] offered as evidence of *mechanical action*, in most cases demonstrate the effect of pH upon peptic activity. For instance, the frog-leg immersion experiments are an example of pH effect. Dragstedt and Matthews[6] found that the digestive action of gastric juice roughly is proportional to the concentration of free HCl, and relatively independent of the concentration of pepsin. The critical acid point for the digestion of frog's legs, blood supply intact, was found to be 0.15% HCl (pH 1.5), or about 40 cc. of 0.1 N.HCl per 100 cc. of gastric juice.

On the other hand, viscosity experiments offer indirect evidence of mechanical protection. The reports of Miller and Dunbar[7] show that gastric *mucin* has, at a pH of 2, 1½ times the viscosity, and at a pH of 4.98, 2½ times the viscosity of *mucin* at a pH of 7.4. Should mechanical protection be a function of viscosity, gastric *mucin* probably should be somewhat more effective in the treatment of gastric than of duodenal ulcers.

As stated above, Dragstedt and Matthews think the acid factor much more important than is the pepsin. However, one group of workers,[8] has reported an increased pepsin content in the ulcer stomach. In a limited number of observations, we have found a high pepsin content in the morning residual gastric juice of ulcer stomachs, as much as was found in the appetite secretions of these subjects. To rule out pepsin entirely, it would be necessary to find an ulcer developing in the *absence of pepsin*, or healing *failing to occur* when gastric pepsin was totally inhibited. In a recent report by Crandall and Roberts[9] on the effect of *chrondroitin* on peptic ulcers, 45% of a series of 22 cases were relieved of symptoms. They ascribe the improvement to its systemic action. In the light of the "antipeptic" properties of *chrondroitin* recorded later in this paper, we would be inclined to attribute the beneficial results to its local action. It would be interesting to repeat their work, studying at the same time, the curve of peptic activity in relation to the symptom picture.

Commercial gastric *mucin* has been shown to inhibit the action of pepsin. Babkin and Komarov[10] have suggested that the inhibitory effect of commercial mucin may be due to the *mucoitin-sulphuric acid* and some impurities, such as soaps, present in it. The late antipeptic effects, as was shown by them with pure *mucin* isolated from dog's sub-maxillary saliva, was thought to be due to the release of inhibitory substances, such as *mucoitin*—or *chondroitin sulphuric acid*. Their deductions were based upon observations made over a 24 hour period (Mett's tube method). Inhibitions varying from 23 to 75%‡ are described. The greatest inhibitions were shown where a considerable drop in free acid of the samples occurred. When the pH was kept fairly constant, an "antipeptic" power of 25-40% could be noted.

During the course of an investigation of the effects of saliva upon gastric physiology,[11] we carried out a series of observations upon the antipeptic effect of gastric *mucin* in comparison with that of salivary mucus. Because our method eliminates some of the variables offered by the Mett's tube method, and also because other variables were checked, we wish to make the following report.

METHODS

Samples of Wilson's commercial and of washed purified *mucin* were used. As the results were alike for both, only one group will be reported. The calcium salt of *chrondroitin sulphuric acid* 50% pure (barium free) was supplied through the courtesy of Dr. Lathan A. Crandall. The pepsin solution was made from Armour's 1-10,000 spongy pepsin—in a modified Sorensen's *glycine*—NaCl—HCl buffer (pH 2.0). The Gates-Gilman-Cowgill[12] photographic film method was used to determine

*Departments of Physiology and of Chemistry, Northwestern University Dental School and the Department of Medicine, Northwestern University Medical School.

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†Reduce the pH of 50 cc. of a 2% solution of commercial gastric *mucin* from 8 to 4.

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‡75% inhibition, i.e., activity of a 1.0% pepsin solution reduced to that of a 0.25% solution.

peptic activity. Briefly, this consists in exposing the gelatin-silver surface of a specially prepared photographic film to the action of the digesting fluid for a period of ten minutes at a temperature of 25 degrees C. The films are then read colorimetrically against a standard, and the peptic activity computed from a logarithmic plot of color changes produced by various dilutions of a standard pepsin solution.

It is evident that this method avoids at least two of the variables inherent in the Mett's tube method: 1. Auto digestion of pepsin itself. Northrup[13] has shown that a pH of 1.5 pepsin loses about 28% of its activity after 24 hours incubation. 2. In measuring the inhibiting effects of substances, it is possible that after a 24 hr. period of incubation (Mett's tube method) there may be additional inhibition due to the release of cleavage-products of hydrolysis; i.e., in the case of gastric *mucin*, of such inhibitory substances as *mucoitin* or *chrondroitin sulphuric acid*.

In determining the inhibitory influence of commercial gastric *mucin*, the following "time samples" were examined:

1. Immediate: Commercial gastric *mucin* was added to freshly made pepsin solution, pH controlled, and peptic activity was determined immediately by the photographic film method. This was done to measure the immediate antipeptic influence of commercial gastric *mucin*.

2. Three hours' incubation at 37° C.: Commercial gastric *mucin* was added to freshly made pepsin solutions in glass stoppered flasks, and then incubated at 37° C. for three hours. The three hour period was chosen arbitrarily because it was felt the orally administered *mucin* may remain in the stomach for such a period of time. The solutions were then tested for peptic activity.

3. Twenty-four hour incubation at 37° C.: The same procedure was carried out as in (2) increasing the time to 24 hours. This period of time was chosen so that comparisons could be made between the film and Mett's tube method.

The pH of the solutions were taken by the quinhydrone method, before and after adding commercial *mucin*, and before and after incubation. The buffering properties of the solution used were found to control hydrogen-ion concentration within .05 to .1 of a pH.

Powdered egg albumin was added to one group of solutions to determine whether or not the presence of this substrate in the Mett's tubes exerted any influence upon peptic activity.

RESULTS

1. *Immediate Effect of Commercial Gastric Mucin Upon the Action of Pepsin:* In Table 1 is reported the average of results obtained on adding 0.5% gastric *mucin* to several concentrations of freshly made 1-10,000 pepsin solutions as described in 1 under "Methods." It is seen that the *mucin* exerts from 20 to 25% inhibitory effect upon the 1%, 0.5%, 0.25% solutions of pepsin, the concentrations of the latter most frequently found by the authors in the basal secretions of the ulcer-stomach. Osterberg, *et al.*,[9] in determining the effects of various gastric contaminants upon peptic activity, report comparable results. Although it is evident that gastric *mucin* exerts an immediate "antipeptic" effect, it is doubtful if such would be sufficient to appreciably influence the progress of an ulcer.

TABLE 1

The Immediate Inhibiting Influence of Gastric Mucin upon Peptic Activity. (Gelatin Film Method).

Gravimetric % Pepsin	% *Mucin*	% Active Pepsin (film)	% Decrease in Activity Due to *Mucin*
1.00	0.50	0.80	20
0.50	0.50	0.38	25
0.25	0.50	0.20	20

TABLE 2

Effect of Gastric Mucin after 3 Hours Incubation with Pepsin Solution.

Gravimetric % Pepsin	% *Mucin*	% Active Pepsin (film)	% Decrease in Activity Due to *Mucin*
1.0	0.0	0.72	..
1.0	0.5	0.70	0

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TABLE 3

Peptic Activity of a 1% Pepsin Solution After Incubation with Gastric Mucin for 24 Hours—37 Degrees C.

Trial	Gravimetric % Pepsin	% *Mucin*	% Egg Albumin	% Active Pepsin	% Decrease in Activity Due to *Mucin*
No. 3	1.0	0.0	0.0	0.66	..
	1.0	0.5	0.0	0.38	48
No. 7	1.0	0.0	0.0	0.58	..
	1.0	0.5	0.0	0.38	35
No. 12	1.0	0.0	0.0	0.60	..
	1.0	0.5	1.0	0.34	44

Apparently, the inhibitory effect is not due to absorption of pepsin because were this so it would be expected that with a constant *mucin* concentration, the peptic activity of the more dilute solutions of pepsin would show larger percental inhibition.

2. *Activity of Pepsin after Three Hours Incubation with Commercial Gastric Mucin:* In Table 2 the results are shown. No inhibitory effect is seen. We are at a loss to explain why the *immediate* anti-peptic effect should have been lost after three hours.

3. *Does Commercial Gastric Mucin Incubated for 24 Hours with Pepsin Show Greater Inhibitory Influences than Fresh Mucin?* The results obtained in this group of experiments showed more variation than those already reported. In Table 3 are shown two extremes: trials No. 3 and No. 7, inhibitions of 48% and 35%, respectively. This is from 10% to 25% greater than is the immediate inhibitory effect of *mucin*. It is felt that this increase possibly is due to the release of some inhibitory substances as *mucin* is hydrolized, possibly substances similar to *chrondroitin sulphuric acid*. Several experiments run with a 0.3% solution of the calcium salt of *chondroitin sulphuric acid* showed immediate "antipeptic" effect of about 75%. Therefore, it is quite possible that the greater inhibitory effects reported by Babkin and Komarov[10] may have been due to the release of such a substance during the time required for operation of the Mett's tube method.

4. *The Effect of Adding Egg Albumin to Pepsin-Mucin Solution:* The addition of 1 gm. of powdered egg albumin to 100 cc. of pepsin solution incubated for 24 hours (Table 3) did not modify the antipeptic effect of commercial *mucin*. Therefore, it can be assumed that the presence of egg albumin in the Mett's tubes does not contribute a variable to account for the difference of the results obtained by that method as compared with the photographic-film method.

CONCLUSIONS

1. The immediate "antipeptic" effect of commercial gastric *mucin* (pH controlled) is about 20%. After 3 hours incubation in vitro this effect is lost.

2. Commercial gastric *mucin*, incubated for 24 hours at 37 degrees C. in a pepsin solution (pH controlled), develops a greater "antipeptic" effect (35-48%). It is thought that this may be due to the hydrolysis of *mucin*, releasing a substance similar to *mucoitin* or *chondroitin sulphuric acid*.

3. The calcium salt of *chondroitin sulphuric acid* has a marked immediate "antipeptic" effect (about 75%).

4. The results obtained indicate that the Mett's tube method may yield an incomplete picture of the events occurring when the inhibitory influences of a substance are being measured.

ABSTRACTS

ASODA, DR. YOSHIO.

Significance of the Liver in the Metabolism of Lipoid Bodies. Study 1—Change in the Amounts of Lipoid Bodies in the Blood and the Bile in Parenteral Administration of Lecithin to Normal Rabbits—The Japanese Journal of Gastroenterology, Imperial University of Kioto, Japan, Vol. V, No. 4, Dec., 1933, p. 115.

Dr. Asoda states that since the liver plays a part in the metabolism of carbohydrates and of protein, it must, in some way, be concerned also with fat and lipoid bodies. He cites the clinical evidences that when hepatic function is faulty changes occur in blood cholesterol and total fatty acids. Since most observers have limited their investigations to blood studies, and since gall stone incidence and catarrhal icterus appear to bear relationships to defective fat metabolism with resultant imbalance of cholesterol and fatty acids in blood serum, he considers that observations upon the chemical variations in the liver's excretion, *viz*—bile, are warranted as possibly throwing light upon one of the functions of the liver which may be disturbed due to faulty metabolism of fat and lipoid bodies.

In the particular study under discussion, Asoda estimated the amount of lecithin and cholesterol in the blood *and* in the liver bile in the event of disturbance of the hepatic function of rabbits and when a lipoid body, as lecithin, was administered parenterally. The paper reports the results obtained first, when intravenous and subcutaneous injections of lecithin were made in *normal* rabbits.

From his experiments, Asoda feels that the following conclusions are established:

In the case of parenteral administration of lecithin to rabbits:

1. The total fatty acids, total cholesterols and lecithin in the blood increased to some extent and then fell gradually to the normal height. The change was more marked in intravenous than in subcutaneous injection.

So far as each fraction of the lipoid bodies is concerned, the degree of the quantitative change became smaller in the order: lecithin, total fatty acids and total cholesterols.

2. Both the concentration and the amount of lecithin and cholesterol in the hepatic bile were increased hand in hand. The increase was more pronounced in intravenous than in subcutaneous injection, and in lecithin than in cholesterol.

Smithies.

ASODA, DR. YOSHIO.

Significance of the Liver in the Metabolism of Lipoid Bodies. Study 11—On the Metabolism of Lipoid Bodies in Hepatic Disturbance in Rabbits—Ibid—supra—P. 124.

Since Asoda's experimental investigations concerned with intravenous and the subcutaneous injections of lecithin into normal rabbits appeared to prove that such produce quantitative augmentation of the lipoid bodies not only in the blood but also in the bile, the Author investigated the effects of similar procedures when the livers of rabbits definitely were abnormal. He submits a brief review of experimental and clinical investigations where it has been shown that, in various forms of hepatic diseases (gall-stones, cirrhosis, catarrhal icterus), certain *quantitative* alterations of the lipoid bodies have been noted. Asoda quotes Nakatsuka of his own Clinic as having proved that, in case of hepatic poisoning, there is a decrease in the amount of *bile* cholesterol. Lecithin in bile has not been adequately studied.

In the present series of experiments, liver function in rabbits was disturbed by peroral exhibition of *carbon tetrachloride*, by repeated injections with *india ink* and by *ligation of the common bile duct*. The studies appear to warrant the following conclusions:

I. In hepatic disturbance in rabbits:

1. When a poison for hepatic parenchymatous cells is previously administered to rabbits, the lecithin and total cholesterol in the blood are increased in the blood and decreased in the bile.

2. When the hepatic stellate cells are blocked, the lecithin and total cholesterol both in the blood and the bile are not widely different from the normal.

3. When the *choledochus* is ligated, the lecithin and total cholesterol in the blood are simultaneously increased.

II. When lecithin is injected into the vein of a rabbit whose liver has previously been disturbed:

1. The rate of diminution of the lecithin in the blood is slowed down in all the three forms of hepatic disturbance mentioned above, but especially in the case of injection of india ink.

2. No increase in lecithin and total cholesterol is found in the bile in any of the three forms of hepatic injury.

III. From the results obtained it is concluded that:

1. The liver plays a part in the regulation of blood-lecithin by dealing with increased lecithin in the blood.

2. The regulation of increased lecithin in the blood comprises two factors, (1) the excretion of lecithin from the bile by the liver and (2) the action of fixing the lecithin in the blood exerted by the reticulo-endothelial cells.

Smithies.

PEREZ, G.

Le modificazioni anatomiche della cistifellea e le variazioni della flora batterica biliare, nella colecisto-gastro-enteroanastomosi (Anatomic modifications of the gall-bladder and variations of the biliary bacterial flora in cholecysto-gastro-enteroanastomosis) Policlinico, 41:40-51, January 15, 1934.

Experimental biliary anastomosis in the dog was attended with the danger of immediate, grave, ascending infection, which led to the death of the animal in 17% of the cases. When the animals survived the operation, the cystic bile was constantly contaminated with pathogenic germs, whatever the type of anastomosis or the segment of the gastro-enteric tube conjoined. In the fatal cases, large anastomotic openings were found which had permitted the reflux of gastro-enteric contents into the gall-bladder. In the dogs sacrificed after a period of survival, ordinary *stomata* of small dimensions were present. Apparently the gravity of the infections was in direct relation to the size of the artificial communication created. The coli bacteria were found most commonly after anastomosis. The common pyogenic germs (staphylococcus and then streptococcus) were next in order. The bacterial flora tended to diminish progressively as the length of the post-operative period increased.

The cholecysto-gastro-enteric anastomosis modified notably the anatomic configuration of the gall-bladder. Macroscopically the gall-bladder lost the form and character of a biliary reservoir, being transformed into a choledochus-like canal by its new office of emptying the bile directly. Histologically, there were signs of inflammation, localized largely in the mucosa and in the lymphatic zone of the neostoma. Such inflammatory signs, however, disappeared with time, and the necrosis of the mucosa was replaced some three months after operation by a regeneration of hyperplastic type from the contiguous healthy mucosa. The cystic contents were constantly invaded by germs, however, and the biliary tract as reconstructed should be considered a *locus minoris resistentiae* for the development of infection, ascending or descending.

S. M. Mc.

BICKEL, A. AND WAGNER, H. I.

The Mechanism of Secretion of the Small Bowel in the Human. Archives f. Verdauungskrankheiten, January, 1934, Vol. 55, No. 1-2.

The authors conducted investigations in this respect on a resected portion of the ileum used for implantation in a case of atresia vaginae. This is one of the very limited cases where such studies were undertaken on humans in contrast to numerous other experiments on dogs with the well known Thiery's ileum fistula. The secretory mechanism is regulated partly by neuro-reflectory and partly by chemical agents. Stimuli for secretion in the small guts are due to the so-called absolute reflex factors in animals, while in the human an additional factor, namely that of a psycho-physiological response, is added. The latter is brought on by processes in the cerebrum giving a possibility thus to explain secretory neuroses. Numerous experimentations by instillation of different agents into the vagina such as protein (meat extracts), butter, carbohydrates, alcohol, etc., have shown that the latency to produce secretion is considerably shorter in the human than in the animals (2-3 minutes). Kephatogenous origin as a bye-factor in establishing additional secretion of the small intestines is to be found only in humans and this is offered as probably the cause of discrepancies found between the results of human and animal secretions of the small bowels.

M. E. Gabor.

ELMAN, R., AND C. T. ECKERT.

Neutralization of Gastric Acidity following Pyloric Closure. Proc. Soc. Exper. Biol. and Med. 30:1343-1344 (June) 1933.

In previous experiments from this laboratory it was shown that the neutralization of gastric acidity, studied by means of an acid test meal, was definitely accelerated by division of the pyloric sphincter. The present experiments show that closing the pylorus partially or completely, produces the opposite effect, i.e., a delay or complete absence of neutralization of the acid test meal.

These experiments add further evidence to the idea previously expressed that there is an actual pyloric control of gastric acidity presumably because the sphincter influences the degree of regurgitation of alkaline duodenal contents particularly pancreatic juice into the stomach. Of additional interest is the finding in many of the experiments of hyperemia of the gastric mucosa and definite inflammatory changes in the duodenum most marked just distal to the partly occluded pylorus. In one dog a perforated ulcer at this point, with death from peritonitis, was found.

L. T. C.

SECTION III—*Nutrition*

MORTALITY IN DIABETIC CHILDREN*

By
HENRY J. JOHN, M.D.
CLEVELAND, OHIO

MORTALITY in diabetic children in the pre-insulin era was very high indeed. One needs but to look at Chart I to see the tremendous difference insulin has made in the mortality of children before and after the insulin era. In this particular field, insulin completely has transformed the situation of a hopeless outlook into a most hopeful outlook. The situation is getting better each year with the spread of knowledge

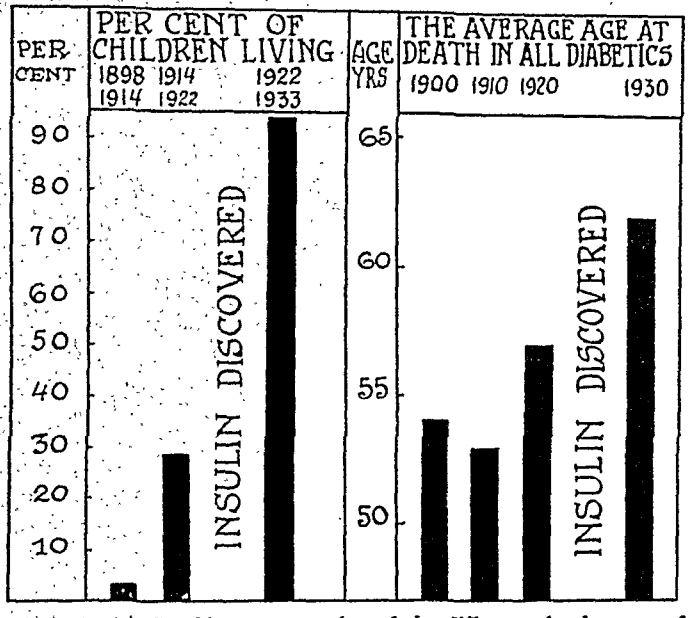


Chart 1—(a) Graphic representation of the difference in the span of life of diabetic children in the pre- and post-insulin era, and (b) the increase in the length of life in adults in the post-insulin era.

as to the proper use of insulin and the crowding out of the idea that insulin is to be used only as a last resort. Quite the contrary, especially in dealing with children, insulin should be used in the earliest possible moment after the diagnosis has been made so as to stop the degenerative process in the pancreas as soon as possible. I give insulin to my children patients in my office, as soon as the diagnosis of diabetes is made—particularly if they have high blood sugar and acidosis—so that not even the few hours are lost that elapse between the time the patient leaves the office and treatment is started in the hospital. One does not lose any time in giving anti-diphtheritic serum when once he makes a diagnosis of diphtheria. This procedure too, has not happened over night but has been a gradual process in the education of medical men. *The giving of insulin in an acute stage of* diabetes in a child is equally important.

In spite of the fact that we still deal with a certain mortality in diabetic children, most children live. In reviewing a group of diabetic children under my care from 1920 to 1934, a period which includes a couple of years in the pre-insulin era, I found that among 214 children (including patients up to 20 years of age), 186 (87%) are living and 28 (13%) are dead. (Table 1). This table includes all the children whom I have seen and treated, but the mortality does not represent a mortality which happened under my care, for such a mortality was included in five children: one died of a postsurgical, adrenal insufficiency (one adrenal completely fibrosed at postmortem, the other presented acute hemorrhage throughout the gland) and in addition a thyroid crisis, as he was suffering from severe hyperthyroidism; two died in coma in the pre-insulin era; two more died in coma, they having been brought into the hospital *in extremis*. The remainder of the twenty-three children died at home. *most of them in rural districts where the family physician* did not have adequate facilities for continued observation and, dependent upon such, modifying their care.

In spite of this, the large majority of children is living, as Table 1 indicates, and of the 186 children living, forty-eight (25.8%) have had their diabetes ten or more years. In fact, in just two more years, there will be eighty-eight of

TABLE 1

The Age at Onset and the Length of Diabetes.

BOYS AND GIRLS

(John)

	Onset Years	Duration of Diabetes in Years															Total	
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Living	1	...	...	...	...	1	...	...	1	...	1	...	1	...	...	...	...	3
	2	...	...	1	...	1	1	...	3	...	2	2	...	1	...	...	...	11
	3	1	1	...	2	...	...	2	...	1	...	1	...	...	...	...	...	8
	4	...	...	1	1	...	1	2	1	1	1	...	...	1	...	...	...	9
	5	...	...	2	...	4	4	...	...	...	...	1	1	...	...	...	...	12
	6	...	1	1	...	...	...	1	...	...	...	...	1	1	...	...	...	5
	7	...	1	...	2	1	...	...	...	...	...	...	...	...	1	...	...	5
	8	...	1	3	1	1	3	...	2	1	1	2	...	1	...	...	...	16
	9	...	...	1	2	...	...	...	...	...	...	...	...	1	...	...	...	4
	10	...	...	1	1	1	1	...	...	3	...	...	...	1	1	...	...	9
	11	...	1	...	...	1	1	...	2	1	1	1	2	...	...	...	...	10
	12	...	1	...	1	4	2	2	1	2	...	...	...	...	...	...	...	13
	13	...	1	1	...	1	1	...	3	2	1	1	1	...	...	...	1	13
	14	...	2	1	...	1	...	1	2	...	1	...	...	...	...	...	...	8
	15	...	...	1	1	1	...	...	2	1	...	...	...	1	1	...	...	8
	16	...	...	...	...	...	1	...	1	3	...	1	...	1	...	...	...	7
	17	...	...	1	3	2	...	...	1	1	1	...	1	1	2	...	...	13
	18	...	3	...	3	...	...	2	4	...	1	...	1	2	2	...	...	18
	19	...	1	...	...	1	2	1	...	...	...	...	...	...	...	...	...	5
	20	...	...	...	1	2	4	...	...	...	...	2	...	...	...	...	...	9
	Total	1	13	14	18	20	20	12	24	16	10	11	8	11	7	...	1	186
Died	1	1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	3	1	...	...	...	...	1	1	1	...	...	...	...	...	...	...	...	3
	4	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	5	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	6	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	7	1	...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	2
	8	...	...	...	...	...	...	...	...	1	...	...	...	...	...	...	...	1
	10	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	11	1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	12	1	...	...	...	...	...	...	...	...	...	...	1	...	...	...	...	2
	13	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	14	2	...	1	...	1	...	...	...	...	...	...	...	...	...	...	...	4
	15	...	...	...	...	...	...	1	...	...	...	...	...	...	...	...	...	1
	16	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	17	1	...	...	...	...	...	1	...	...	...	...	...	...	...	...	...	2
	18	2	...	...	...	...	...	...	1	...	...	...	...	...	...	...	...	3
	19	1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	20	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1
	Total	11	3	4	...	2	1	3	2	1	...	...	1	...	...	...	...	28

*Received for publication, March 28, 1934.

these (50%), who will have had their diabetes ten years or more. This situation is most encouraging. There should be little mortality in this group, for the longer a child has had diabetes, the better are his chances for living. This is well-illustrated in Table 1, which shows that of the twenty-eight children who died, eleven (39.2%) died in the first year of their diabetes, and eighteen (64.2%) died in the first three years of their diabetes. Of the eighteen children who died in coma, eleven (61%) died in the first three years of their diabetes. After that early experience, it is observed that coma appears but sporadically.

In Table 2, I have classified the *individual patients* who died, according to (1) the cause of death, (2) sex, and (3) the

TABLE 2

*Mortality in a Series of 214 Diabetic Children**

(John)

No.	Age in Years at		Sex		Cause of Death								Duration of Diabetes in Years
	Onset	Death	M	F	Coma	Tuberculosis	Adrenal Denervation	Killed in Accident	Appendectomy	Septicemia	Otitis Media	Uremic Coma	
1	16	19	√		√								3.
2	18	23	√			√							5
3	20	21	√				√P.M.						1.
4	14	18	√						√				4.
5	14	14	√		√								.1
6	11	11	√		√								.1
7	4	10	√		√								6.
8	17	23		√	√								6.
9	14	16	√		√								2.
10	7	7	√		√								.1
11	5	7	√		√								2.
12	1	1	√		√								.3
13	5	6	√					√					1.
14	10	11	√		√								1.
15	7	11	√						√				4
16	12	12	√		√								.5
17	4	10	√		√P.M.								4.
18	12	13	√		√								1.
19	4	11	√							√			7.
20	19	20		√	√								1.
21	3	4		√	√								1.
22	15	21		√		√P.M.							6.
23	18	18		√							√		.5
24	8	16		√	√P.M.								8.
25	17	17		√	√								.00
26	14	15		√	√								1
27	12	20		√		√							8.
28	18	18		√								√	.2
Total			18	10	18	3	1	1	2	1	1	1	

Total deaths 28. Of these I took care of 5. Cause of death of these:
No. 3. Adrenal insufficiency after denervation.
5. Coma, preinsulin era.
6. Coma, preinsulin era, brought in last stage.
24. Coma, brought in last stage of coma.
25. Coma, died one hour after reaching hospital.

*Includes preinsulin era—ages 1-20 years.
P.M.—Postmortem.

duration of the diabetes. It is quite obvious that coma ranks first, causing eighteen (64.2%) of the twenty-eight deaths. Many of these deaths, as I have already indicated, were unnecessary and probably would not happen today even in the same localities and environments.

Doctors still have a fear of "insulin reactions" when the child is vomiting and not eating, and forget that these symptoms usually mean severe acidosis, a condition in which the insulin dosage should be doubled or tripled. Acidosis is still mistaken for acute appendicitis and children are rushed to the operating table, or infections occur and, when the child begins to vomit, the family promptly discontinues all insulin. In case 19 (Table 2) four teeth were extracted and septicemia followed. Such occurrences, fortunately, gradually are becoming past history, and the future will have much better *data* to offer.

In Table 3, I have reviewed certain mortality series which are available in the literature. One must evaluate such figures by taking into consideration whether they are from the pre-insulin era, or of the insulin era, or combinations of both periods. Thus, when we consider Joslin's entire series of 750 children, the mortality is 28.9%; when this series is separated

TABLE 3

Mortality in Diabetic Children

Author	Total Cases of Diabetes	Number Cases Died	Mort. Per Cent	Died in Coma	Per Cent	Died of Tuberculosis	Per Cent
Joslin—White Preinsulin and Insulin era...	750	217	28.9				
Joslin—White Insulin era...	587	54	9.3	36	66.6	1	1.85
Mulholland Insulin era...	40	13	32.5	8	61.	2	15.4
John Preinsulin and Insulin era...	214	28	13	18	64.	3	10.6
Escudero Insulin era...	34	4	11.76	0	0	2	50.0

and only the insulin era is reviewed, there is a mortality of but 9.3%. Since the children of the insulin era are nearly 75% of his total number, it would indicate that the mortality of the pre-insulin era was 93%, in which circumstance the insulin era figures are even more striking.

Mulholland, in a small series in the insulin era, records a high mortality, namely, 32%. However, the series is too small, for thus computed each death counts up 2.5%. This is not a true picture of conditions; besides we know not the reason for this, as there are many extraneous factors which influence the mortality rate. Joslin's figures too are quite different when he considers merely the mortality of those who were under his own care at the time of death, and so it is with all medical workers.

In my own series of 214 children the mortality rate was 13%. I have already presented a detailed analysis of these deaths.

When we consider deaths from coma, (Table 3) my figures run quite parallel with those of others, namely, 66.6%, 61% and 64% of deaths from coma, with the exception of Escudero's data which exhibit none. This illustrates the heavy toll which had to be paid in the past to this factor in spite of the insulin era. Mortality statistics for coma in children will improve *only* when *acidosis* is *recognized early* and *adequately combated.* Mortality from coma will always be high when the treatment is started late, regardless of who treats the case. This point needs to be stressed heavily by medical educators in instructing medical youth, which is becoming better and better prepared to deal with the problem each year.

There is only one other condition which I tabulated in Table 3, viz: tuberculosis. Its incidence in diabetic mortality still is high—somewhere between 10 and 15%.

In case 22, Table 2, a girl who developed diabetes at the age of fifteen, was married at eighteen and at nineteen had a healthy baby. The baby survived his mother, who died at the age of twenty-one of acute, disseminated, pulmonary tuberculosis.

Such, then, briefly is the history of diabetic children in the pre-insulin and the insulin eras. I dare say that statistics starting from 1930 will present a much brighter picture. The period prior to 1930, covered the beginning of a new era and the study of a new problem. From 1930 on, we should see results of a problem which has been worked out and placed on a sound basis: even the public is better educated today than it was in 1922 and it seeks medical aid much earlier than formerly when complications arise so that now a medical man has a better opportunity to deal early with emergencies.

SUMMARY

1. A review is presented of 214 cases of diabetes in children, under my care from 1920 to 1934, which period goes back

two years into the pre-insulin era. A gross mortality of 13% is recorded.

2. Of the 186 children living, forty-eight (25.8%) have had their diabetes ten or more years.

3. Of the twenty-eight children who died, 39.2% died in the first year of their diabetes; 64.2% died in the first three years of their diabetes.

4. In children, deaths from coma as given in the literature, run about 63% of the total mortality.

5. Deaths from tuberculosis, in my own series, were 10.6%.

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THE EFFECT UPON THE GASTRIC JUICE SECRETION OF VARIOUS COOKED PREPARATIONS OF HADDOCK (*Melanogrammus aeglefinus*) AND OF LOBSTER (*Homarus americanus*)*

By

A. ALLEY, M. D.

MONTREAL, Q., CANADA

IT IS important to know for the complete evaluation of the nutritional values of fish, as of any other food, not only its content of protein, carbohydrate, fat and vitamines but also its effect on the gastro-intestinal tract. Food, in turn, will be properly digested and prepared for absorption only if the secretory and motor apparatus functions adequately. Palatability of the food and the possession of certain chemical (extractives, etc.), and physical (solids, liquids, etc.), properties are very necessary to the adequate function of the gastric glands and proper motor activity of the stomach. Products of the digestive disintegration of food substances ("natural chemical stimuli") also are known to influence the motility of the stomach (Babkin, 1928).

Data are scarce concerning the effect of different fish and of different fish preparations on the secretion of the gastric glands. Gordeieff (1906) using a dog with a Pavlov pouch, compared the effect on the gastric secretion of salted herring and of herring from which the salt had been previously washed. The former stimulated three times as large a secretion, although it was given in equal amounts, as the latter. The salt-freed herring also was shown to possess strong secretagogue properties because it stimulated a secretion equal to that of an equivalent amount of raw meat. Boldyreff, working on Pavlov pouch dogs, demonstrated that his fish extract ("fish *bouillon*") stimulated a much greater secretion of gastric juice than his meat extract ("meat *bouillon*"). He showed the same to be true of the products of fish and meat digestion and also true of equivalent amounts of meat and fish. Boldyreff observed an especially large secretion when he introduced a small fish, *Coltus gobio*, or a fish "*bouillon*" from this and other small fish into the stomach of a dog. "*Bouillon*" from the larger species possessed a smaller secretagogue power than that of the small species. This decrease is possibly explained by the fact that there was a smaller proportion of skin on the raw food from which the extract had been prepared. Komarov in 1931, using a dog with a Pavlov pouch obtained an 85% increase in volume of gastric secretion on haddock broth to which the skin was added as compared with meat broth or haddock broth without skin.

An investigation was carried out by Alley (1932) on the effect of various fish (cod, haddock, mackerel, lobster) and beef heart on gastric secretion. The juice was collected from a pouch built from the lesser curvature region of a dog's stomach (Armour 1930). The Armour pouch was used rather than the Pavlov pouch because it was thought important to know the type of juice with which the mucous membrane of the lesser curvature region would come into contact. Such knowledge is important for the understanding of both the normal and the pathological conditions of the stomach. Only the second or chemical phase of the gastric secretion was studied by introducing the different foods directly into the stomach through the gastric fistula. It was found that the fish (cod, haddock and mackerel) was as strong a stimulus of the acid and fluid of the gastric secretion as was beef heart, while lobster was a much stronger stimulus. The peptic power of the juice secreted on haddock and lobster was higher than that on cod and beef and much higher than that on mackerel, probably due to the high content of fat in the mackerel. Cod, haddock and lobster remained in the stomach as long as beef heart while mackerel remained longer. Results from the above experiments gave us a fair understanding of the effect of these substances on the secretory and motor functions of the stomach. Their value in dietetics, however, was not complete since only the chemical phase of gastric secretion was studied and the fish was given in a raw state. In the present investigation it was decided to give the fish to the dog by mouth and to prepare it according to different culinary procedures.

METHOD

A dog with a pouch from the lesser curvature region (Armour pouch) was used. The food given was boiled, baked, fried and smoked haddock, boiled lobster, and raw beef heart (*control*). 250 grams were given broken in small pieces approximately 5 c.cm. in size. The haddock was prepared by baking in an oven at 360° F. for half an hour, or boiling in water for 7 minutes, or frying in butter a centimeter deep in a pan for 15 minutes. For the smoked haddock, "finnan haddie" was used. The lobster was boiled for one-half hour. The beef heart was minced and all visible fat removed.

The experiment always started when the gastric glands were resting, i.e., no secretion flowed from the pouch. The secretion from the Armour pouch was collected hourly and filtered immediately. The free and total acidity were determined by titration, Topfers reagent and phenolphthalein respectively being used as indicators. Nirenstein and Schiffs' modification of Mett's method was used for the determination of peptic activity. The content of dissolved mucin was determined by the increase in the reducing power of the gastric juice after it had been hydrolyzed by boiling with 2 Normal H_2SO_4 for 2½ hours. Hagedorn and Jensen's method was used for determining the reducing power. The amount of glucose (read from the Hagedorn and Jensen Tables) multiplied by eight gives the content of dissolved mucin (Webster and Komarov 1932). Between experiments, the animal was fed on a constant diet of oatmeal porridge, raw beef heart, milk, cod liver oil, salt and water.

RESULTS

The course of the volumes of secretion after the different preparations of haddock, showed some striking variations (Table 1 and Figures 1 and 2). The first hour secretions were very close, being within 1 c.c. of each other. The second hour secretions however varied greatly: that of boiled haddock showed a considerable drop, baked and fried fish a smaller drop, while the secretion of smoked fish remained quite high. Throughout the remaining three hours there was a continual

*Department of Physiology, McGill University, Montreal, Canada
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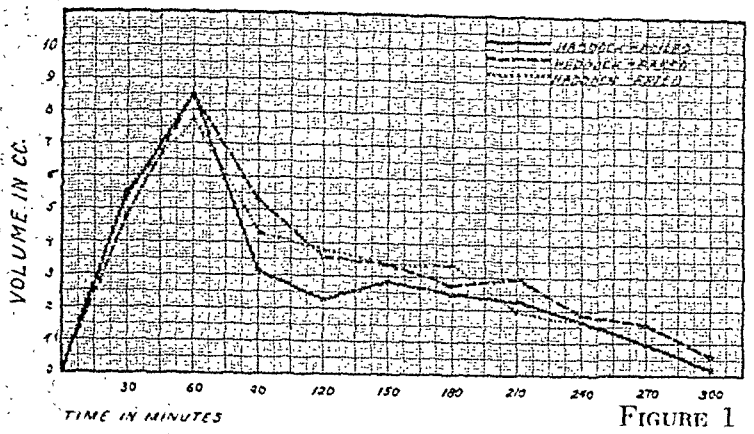


FIGURE 1

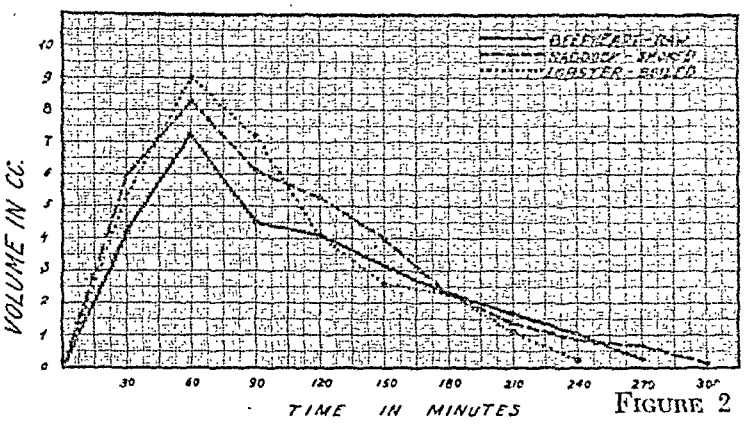


FIGURE 2

TABLE 1

Volume of secretion in c.c. for successive hour and half-hour periods following ingestion of food.

Hours	Haddock Boiled		Haddock Baked		Haddock Fried		Haddock Smoked		Lobster Boiled		Beef heart Raw	
	Per Half Hour	Per Hour	Per Half Hour	Per Hour	Per Half Hour	Per Hour	Per Half Hour	Per Hour	Per Half Hour	Per Hour	Per Half Hour	Per Hour
1	5.4 8.5	13.9	4.8 8.5	13.3	5.5 7.7	13.2	6.0 8.3	14.3	5.1 9.0	14.1	4.2 7.2	11.4
2	3.1 2.3	5.4	5.3 3.6	8.9	4.3 3.8	8.1	6.1 5.3	11.4	7.2 4.1	11.3	4.5 4.1	8.6
3	2.9 2.5	5.4	3.4 2.8	6.2	3.4 3.4	6.8	4.0 2.3	6.3	2.6 2.3	4.9	3.1 2.3	5.4
4	2.3 1.7	4.0	3.0 1.8	4.8	2.0 1.6	3.6	1.4 0.9	3.3	1.1 0.2	1.3	1.7 1.0	2.7
5	1.0 0.2	1.2	1.6 0.6	2.2	1.0 0.2	1.2	0.7 0.1	0.8	. .	.	0.3 .	0.3
Total Volume	29.9		35.4		32.9		35.0		32.1		28.1	
Duration of Secretion	4 h. 40 min.		4 h. 55 min.		4 h. 25 min.		4 h. 23 min.		3 h. 45 min.		4 h. 15 min.	

fall in secretion with all preparations except in the third hour of boiled haddock which remained the same as in the second hour. The baked fish gave the highest total volume and boiled fish the lowest. The durations of secretion varied considerably, that of baked fish being the most prolonged. The secretion on boiled lobster was remarkably different from that on boiled haddock (Table 1). The powerful effect of the lobster may be observed from the fact the volume of secretion in the second hour remained high while that of boiled haddock dropped greatly in that period. The raw beef heart gave less secretion in the first hour, shorter duration and less total volume than the cooked fish.

TABLE 2

Total and free acidity; average concentration of acid in milli-equivalents per litre for successive hourly periods.

Hours	Haddock Boiled		Haddock Baked		Haddock Fried		Haddock Smoked		Beef heart Raw		Lobster Boiled	
	Total	Free	Total	Free	Total	Free	Total	Free	Total	Free	Total	Free
1	146	108	141	103	146	102	152	101	142	102	152	100
2	147	108	147	105	150	100	159	113	147	105	157	115
3	143	101	140	97	142	93	146	97	136	98	139	91
4	134	94	130	89	126	79	134	85	124	81	115	67
Average Acidity	144	105	142	101	144	97	148	100	142	105	147	101

The total acidity (Table 2) was the highest with lobster and smoked fish while baked fish gave the lowest. It is of interest to note that lobster, fried and smoked fish gave relatively low free acidities.

TABLE 3

Peptic power and output of pepsin calculated from Mells units for successive hourly periods.

Hours	Haddock Boiled		Haddock Baked		Haddock Fried		Haddock Smoked		Beef heart Raw		Lobster Boiled	
	Power	Output	Power	Output	Power	Output	Power	Output	Power	Output	Power	Output
1	252	3574	256	3401	277	3666	264	3672	258	2913	295	4247
2	198	1067	258	2306	203	1656	181	2096	261	2213	296	3353
3	199	1019	293	1815	189	1279	191	1206	253	1381	443	2137
4	236	956	321	1571	285	1009	344	748	329	852	570	723
Total Output		6616		9096		7610		7722		7389		10160
Average Power	230		272		240		225		262		323	

The pepsin (Table 3) is seen to be the highest after boiled lobster in both power and output followed closely by baked fish. Salted and fried fish gave somewhat lower but fairly similar figures for pepsin. Boiled fish gave the smallest output even though the concentration was not the lowest.

TABLE 4

Concentration of dissolved mucin in mg. per cent and its output in mg. for successive hourly periods.

Hours	Haddock Boiled		Haddock Baked		Haddock Fried		Haddock Smoked		Beef heart Raw		Lobster Boiled	
	Conc.	Output	Conc.	Output	Conc.	Output	Conc.	Output	Conc.	Output	Conc.	Output
1	96.8	13.7	100.8	14.0	84.8	11.1	59.2	8.4	93.6	10.2	96.0	13.0
2	82.4	4.0	99.2	8.8	96.0	7.7	74.2	8.5	86.4	7.4	102.4	11.1
3	92.8	4.7	106.4	6.5	104.8	6.6	68.8	4.4	105.6	5.3	160.0	8.8
4	96.8	4.0	131.2	6.0	152.8	5.6	52.8	1.6	112.0	3.8	192.0	2.8
Total Output		26.4		35.3		31.0		22.9		26.7		35.7
Average Concentration	93.6		103.2		97.6		67.2		95.2		104.0	

Dissolved mucin (Table 4) followed a course similar to that of pepsin but did not show such a respectively great increase with lobster as a stimulus.

DISCUSSION

From the above results it will be seen (Table 5) that the various preparations elicited very different responses from

TABLE 5

Average figures for the secretion during four hours after ingestion of the different food substances.

Food	No. of Experiments	Gastric Secretion							
		Duration Average	Vol'me	Acidity Average		Pepsin		Mucin	
			Total Ave. c.c.	Total	Free	Concen. Calculated from Mett's Units	Output	Conc.	Output
		hrs. mins.		m.eq./lit				mg.%	mg.
Haddock:									
Boiled	3	4 40	29.9	144	105	230	661	93.6	26.4
Baked	3	4 55	35.4	142	101	272	9096	103.2	35.3
Fried	3	4 25	32.9	144	97	240	7610	97.6	31.0
Smoked	2	4 23	35.1	148	100	225	7722	67.2	22.9
Lobster:									
Boiled	2	3 45	32.4	147	101	323	10460	101.0	35.0
Beef heart:									
Raw	3	4 15	28.4	142	105	262	7389	95.2	26.7

the gastric glands. Of the haddock preparations the baked muscle was much the strongest stimulus giving a secretion of the greatest duration and volume and highest pepsin and mucin content. The free acidity of the baked fish secretion was the lowest. The boiled fish with its water-soluble constituents greatly reduced became a weaker stimulus than did baked haddock, the secretion showing a decrease in volume, pepsin and mucin. The smoked fish caused a greatly increased total acidity but lower peptic power and mucin content. The effect of the fried fish was not greatly decreased by the butter causing a low free acidity and somewhat reduced pepsin and mucin. Boiled lobster is shown to be a much more powerful stimulus of the gastric glands than is boiled haddock as demonstrated by its higher volume, total acidity, pepsin and mucin of the secretion.

Our present knowledge of the action of different secretagogues on the gastric glands can only explain in part the difference in effect of the various fish preparations. Fish, during the process of boiling, loses its water-soluble constituents such as inorganic salts and other extractives—substances which are powerful stimulants of the gastric glands— and with their loss a somewhat diminished secretion occurs as compared with that of the other fish preparations. During the baking of fish, roast products are formed which not only stimulate the taste but also probably act as secretagogues to the gastric glands; this may explain the greater secretion when the subject is fed on baked fish. The secretion on fried fish seemed to be little affected by the fat present, as the free acidity, peptic power or concentration of mucin were only slightly depressed. The effect of the smoked fish may be explained chiefly by the presence of salt which not only increased the amount of secretion but also lowered the peptic power of gastric juice (Gordeieff). In spite of the fact that a great deal of juice was lost on opening the shell of boiled lobsters, this food was still a very strong stimulus—much stronger than was boiled haddock. It is known to have a much higher ash content than has haddock (McLester, 1931). The duration of secretion was much shorter after lobster than after haddock.

It is believed that the data reported in this investigation may be of use in the elaboration of proper diets when a decrease or increase of gastric secretion is desired in an effort to aid various disorders of gastric function, especially those of the lesser curvature.

SUMMARY

From the results obtained on the above experimental animal it is seen that haddock-muscle, prepared in various ways, stimulated different types of gastric secretion. Baked haddock was the strongest stimulus, especially for fluid, pepsin and mucin. Of the three remaining preparations, boiled, fried and salted haddock, boiled haddock stimulated a lower volume and smaller pepsin output, although the secretion continued somewhat longer in duration. Little inhibition was noticed from the fat of the fried fish. Smoked fish was a strong stimulus to fluid and acid production but weak for pepsin and mucin concentration. Lobster, in spite of the resulting secretion being of shorter duration was a much stronger stimulus for the volume of secretion as well as for acid, pepsin and mucin content than was the boiled haddock.

The writer wishes to thank the Biological Board of Canada for the excellent facilities provided for the carrying out of this work at the Atlantic Biological Station, St. Andrews, N.B., and Dr. B. P. Babkin for his valuable help and criticism. The writer also wishes to thank the Banting Research Foundation for defraying some of the expenses by supplying the experimental animal and certain apparatus.

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ABSTRACTS

CONNERY, JOSEPH E., M.D., AND GOLDWATER, LEONARD J., M.D., NEW YORK, N. Y.

Therapy in Pernicious Anemia: observations covering two years of continued use. Annals of Internal Medicine, March, 1934, p. 1117.

Results of the continued parenteral administration of liver extract to a series of patients with pernicious anemia, some of whom have been under this form of treatment for as long as two years.

The extract used for the first six months was of such concentration that 5 c.c. contained the material derived from 100 gm. of liver. Later the concentration was increased so that the same amount of active material was contained in 3 c.c. of solution. No liver, liver extract, kidney or other specific anti-anemic substance was eaten during the study.

Weekly intramuscular injections were given for a period of six months and the condition was regarded as satisfactory if the red cell count was about 4.5 million or above it, if neurologic lesions, already present, had shown no progression nor new ones become manifest, if there had been no recurrence of signs or symptoms referable to the gastro-intestinal tract, and if the patient felt well.

Some of the patients were then given the injections every second week while some were continued on weekly doses another six months, and if their conditions were satisfactory injections were given every three or four weeks.

With one exception a count of 5 million was not maintained but in the majority 4.5 millions or above was attained. In comparing these figures with Murphy's, half of the patients were in greatly reduced circumstances and with three exceptions no iron or whole liver was taken.

Of the 38 patients 21 maintained a hemoglobin level of 13 gm. or more per 100 c.c. of blood, 17 ranged between 10 and 13 gm. per 100 c.c. of blood.

The patients were divided into two groups; those who had received other forms of therapy and were in remission, and those who had not been given previous treatment. After the latter group had reached normal red cell counts the course was the same as in the first group.

Neurologic manifestations if present at the beginning did not progress nor did any symptoms of involvement of the nervous system appear in those who were free from them at the start. Some regained locomotion and some returned to occupations.

Abnormal deep tendon reflexes and impaired vibratory and position sense showed no improvement. An occasional temporary return of acro-paresthesia or glossitis was noted.

In 2000 intramuscular injections no severe reactions followed nor was there a single infection.

Pain in the site of injection was not severe and the patients did not wish to return to oral therapy.

Allen Jones.

SECTION IV—*Roentgenology*

X-RAY'S CONTRIBUTION TO THE DIAGNOSIS OF THE "ACUTE ABDOMEN"*

By

WILLIAM H. STEWART, M.D. *and* H. EARL ILLICK, M. D.

NEW YORK CITY, NEW YORK

AT FIRST thought, one might question whether the roentgen examination of any patient with an "acute abdomen" could be of value. The term "acute abdomen," has been coined by the surgeon for those cases which come within his province where immediate surgery is deemed necessary. Usually, in such instances, by the time that they have been diagnosed as "acute abdomens," the only question remaining is how soon need operation be performed.

More and more, however, the modern surgical tendency is to be as sure of the diagnosis as possible *before* the operative procedure actually is carried out so that the method of approach and the surgical treatment may be most efficacious. There are certain lesions in which roentgen examination particularly is helpful; in the actual diagnosis or in the differentiation of lesions, more and more is the surgeon depending upon the X-ray for aid.

Without much additional discomfort to the patient and while preparation is being made for operation, certain important information may be obtained by the alert surgeon which information will help him greatly in the proper management of his patient. The X-ray may aid not only *positively* in confirming a suspected diagnosis but also *negatively* in ruling out certain lesions which might add confusion in a case. In certain instances of trauma, resulting in the production of internal injury, without the facts obtainable by roentgen study "watchful waiting" may result in loss of the patient just as certainly as might hasty operations. Frequently, when all the information possible to obtain is before the surgeon, he may decide that it is wisest not to operate at all and that the patient has the best chance for recovery with medical treatment alone.

In discussing the various lesions in which the X-ray may be of assistance in the diagnosis of the "acute abdomen," it it would seem useful to group them into classes as:

1. *Obstruction*—caused by intestinal adhesions, hernia, concretions, malignancy;
2. *Perforation of:* duodenal ulcer, gastric ulcer, diverticulum;
3. *Rupture of* kidney;
4. *Inflammation—resulting in* acute cholecystitis, acute appendicitis;
5. *Intussusception;*
6. *Colic*-biliary, urinary;
7. *Hemorrhage*—from ulcer, malignancy.

I. INTESTINAL OBSTRUCTION

When the clinician is confronted with a patient in whom the question of obstruction arises, the X-ray examination may be of considerable value. The first procedure is to obtain what is called a "flat film," that is a film without the use of any opaque medium either orally or rectally administered. This may be taken with the patient supine, but it is preferable to have the patient erect. As a rule, the patient can be gently placed in a sitting posture at the edge of a bed or stretcher and a film exposed with the tube in front and the film behind or the reverse. At times, one may even fluoroscope such a patient without danger and certain information may be obtained as for example: the *excursion and mobility of the diaphragm.* In the presence of an *obstructed small intestine* from any cause, the "flat film" will show dilated, gas-distended, small intestinal loops which usually criss-cross the abdomen in the so-called "step ladder" or "herring bone" pattern—a finding quite characteristic for small intestinal obstruction. The degree of the distention of the loops depends on the completeness of the obstruction. In the large intestines, the coils of gas-distended colon do not assume

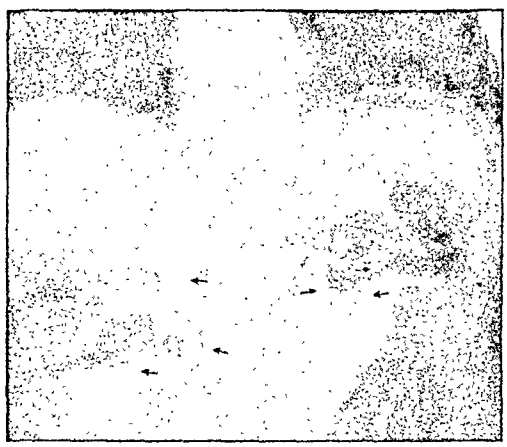


Figure 1—Fluid levels with gas above, demonstrated in acute intestinal obstruction when the patient sits or stands up. The cause of the obstruction was a band of adhesions close to the ileo-cecal valve.

the appearance as described above; more commonly, one finds dilated gas-filled coils and loops corresponding to the general location of the large bowel.

If one has been able to examine the patient in the upright position, he may also be able to show multiple fluid levels, with gas above them (Figure 1). This finding is of extreme importance as a confirmation of a well-established obstructive intestinal lesion.

Usually the first question the surgeon asks is "Where is the obstruction?" It is possible to reply in only a general way. From the roentgenographic standpoint, the location often is difficult to determine inasmuch the distended loops of intestine overlap and overshadow the point of obstruction as well as blot out the cause of the stoppage. At times, the coils of dilated intestine *proximal* to the obstruction may be followed down to the point of constriction although it may be difficult to ascertain the nature of the lesion. However, the clinical history may aid in determining the location and cause of the obstruction. If the case is post-operative, adhesions usually account for the trouble; the character of the operation and the location of the scar are valuable aids in locating the obstruction. If the small intestine is distended and visible in the left side of the abdomen and the patient has had no

*From the Roentgen Laboratories of The Lenox Hill Hospital.
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previous surgical procedure, there is a strong probability of obstruction from appendicular disease, adhesions or



Figure 2—Typical roentgenographic appearance in acute, small intestinal obstruction. The distended, small intestinal coils crisscross the abdomen in a so-called "herringbone" or "step-ladder" appearance. The obstruction was due to an appendicular abscess.

abscess. (Figure 2) Malignancy often is the cause of obstruction in non-operated patients (Figure 3).

It is not usually advisable to give a barium meal better to localize the site of obstruction when the patient already is vomiting and the clinical diagnosis of acute abdominal ob-



Figure 3—Acute, intestinal obstruction with markedly distended coils of small intestine due to an annular cancer of the distal ileum. Patient was apparently well until three weeks ago when she began vomiting following which there were abdominal pain and distension.

struction already has been arrived at: the exact localization of the obstructed area may not be of so much importance as is immediate surgery. Moreover, in an almost completely obstructive lesion, barium may act as a "plug," thus turning the case into one of complete obstruction requiring immediate surgical relief or death rapidly will ensue. If a barium meal should be given it would be advisable to exhibit only a swallow or two of the mixture and then follow this small meal by frequent fluoroscopic and roentgenographic examinations. Such a procedure may be done at the bedside, the films being made with a portable X-ray apparatus. As a rule, it is difficult to localize the exact point of obstruction even after barium has been given. More than once, however, it has been our experience to find that, following a barium meal, an obstruction has become lessened and in some cases of an incompletely obstructive lesion, the patient went on to recovery.

One of the frequent causes of intestinal obstruction is kinking of a loop of gut in a hernial sac or the adhesions resulting from such a lesion. The patient may first be seen by the physician when complaining of the symptoms due to an acute intestinal obstruction: on physical examination hernia may be overlooked and the patient referred for X-ray examination with the belief that there is some cause other than hernia for the intestinal obstruction. It is in such a case as this that the roentgenologist is helped by inquiring whether the patient has, to his knowledge a hernia or "rupture." We distinctly recall one patient in whom a hernia was suspected and an X-ray examination was made at the bedside. It was reported that only very slight gaseous distension of the small intestines was distinguishable in the right lower abdominal quadrant. At operation, the patient had a loop of small



Figure 4—Peculiar shadows of rectal and sigmoid fecaliths causing a partial, intestinal obstruction.

intestines kinked and angulated in a hernia. This was a very early case, the entire duration of symptoms being only a matter of a few hours before the operation was performed. Where a longer interval elapses before the patient is operated upon, the dilated coils may present a typical appearance of intestinal obstruction when a "flat" abdominal X-ray film is exposed.

Our personal experience with *concretions* as a cause of intestinal obstruction is limited to *fecaliths* and *gall stones*. In both, the X-ray examination revealed the lesion. In the first instance, the patient complained of increasing constipation until finally no bowel movements took place no matter what measures were utilized. The patient, as well as the examining physician, made the observation that when she strained, at times, there would be a protrusion of a hard mass from the rectum which mass could easily be pushed back. The roentgen examination demonstrated *four calcified ring-like shadows* thought to be large gall stones. (Figure 4). A gall bladder examination, by means of the Graham test, however, was negative, the gall bladder being beautifully outlined with a normally dense shadow in which there were no visible stones. These four shadows above mentioned proved on direct examination to be huge *fecaliths*.

Frequently, gall stones are a cause of intestinal obstruction and usually can be detected by the X-ray examination. One very interesting case resulted in the demonstration of a large calcified gall stone as the cause of the small intestinal obstruction. There had been a spontaneous cholecystoduodenal fistula and the gall stone had passed down into the terminal ileum about a foot or so from the ileo-cecal valve, resulting in an obstructive lesion which made surgery necessary. The gall stone practically was the size of an average gall bladder. (Figure 5).

Malignancy of the intestinal tract occasionally is the cause of obstruction. It may be gradual in onset or appear with



Figure 5—Partial obstruction to the ileum from a large gallstone; a barium *clysma* was given to exclude any lesion of the colon.

sharp, unsuspected violence with complete stoppage. When malignancy involves the small intestine, one has to depend upon the "flat film" for diagnosis. When its occurrence is gradual the lesion is more difficult to recognize especially if it involves the large intestines; in the latter circumstance, one can resort to the barium *clysma*, with or without air insufflation. When obstruction is sudden, the X-ray findings



Figure 6—Air is present beneath both sides of the diaphragm due to a perforated *gastric ulcer*. The onset of the symptoms occurred less than 24 hours before the roentgenographic examination.

are much the same as those seen when adhesions are the cause.

II. PERFORATION

Gastric and Duodenal Ulcer: When the physician examines a patient in whom there is suspected rupture of an ulcer, usually immediate operation is indicated. Such a case may be examined by X-ray before operative procedure as an aid in the differential diagnosis where one or more common essential signs are lacking. Usually the value of the X-ray consists in demonstrating *free air* beneath the domes of the diaphragm. This is facilitated if the patient is sitting upright or lying on the normal side, the X-ray film then being placed behind the patient. Free air forms a characteristic quarter moon-shaped area outlining the under surface of the dome of the diaphragm on the right side and sometimes the left side as well. (Figures 6 and 7). If this air "bubble" can be demonstrated, perforation of an abdominal viscus: most probably an ulcer of the stomach or of the duodenum is the offending lesion. In rare instances, the examination may be reported "negative" for free air but a ruptured ulcer may be found at operation, nevertheless; hence a negative finding should not be accepted as absolutely ruling out a perforated viscus.

One interesting case, on bedside examination, was found to have a large cavity containing fluid with air above, ap-

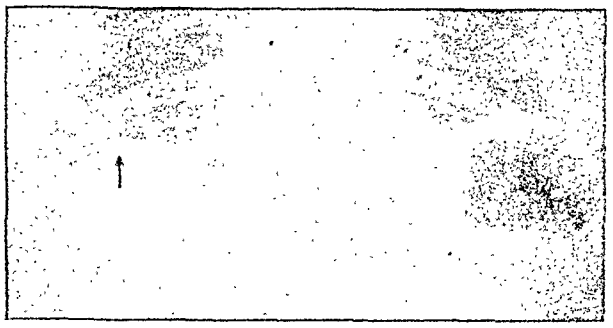


Figure 7—Another example of an acute perforation of a *duodenal ulcer* in which air was demonstrated beneath the diaphragm.

parently corresponding with the lesser peritoneal cavity. This turned out to be an ulcer on the posterior wall, perforated and associated with a large area of localized peritonitis. (Figure 8).

Diverticulosis is a fairly common lesion of the colon and it is not unusual to have patients referred for X-ray examination who are suffering from acute diverticulitis with an obstructive lesion in the distal colon of rather marked degree, even complete. This has been our experience repeatedly in middle-aged or older patients who have an obstruction in the pelvic colon to a barium *clysma*. The tendency is to regard such lesion as malignant but, often, when the patient is re-examined 24 hours later, diverticula are discernable. In fact, we are much more suspicious of an inflammatory, *benign lesion when the obstruction is complete* than when there is a *gaping canalization permitting fluids to pass;* this latter state oftener is characteristic for a cancer.

Occasionally we find an "acute abdomen" due to a ruptured diverticulum which can be recognized by X-ray exam-



Figure 8—Bedside roentgen examination demonstrating a huge, fluid level of an abscess secondary to a perforation of the posterior wall of the duodenum from an ulcer. The onset was sudden, eleven days previously, with severe, epigastric pain.

ination following a barium *clysma;* then the opaque medium passes through the ruptured diverticulum into small fistulous tracts in the wall of the colon or out into the perisigmoid structures where it is walled off in an inflammatory mass: this anomaly can be recognized readily on roentgenograms. (Figure 9).

III. RUPTURE OF THE KIDNEY

There are certain instances of "acute abdomen" where the patient is in shock due to a serious trauma, in which the X-ray examination may be of great assistance. It takes only a few minutes to demonstrate the renal calices and pelvis by means of intravenous urography and thus to rule out a possible ruptured kidney. For example, a man may be involved in a serious automobile accident, may be admitted to the Hospital in shock from obvious acute abdominal distress. The surgical diagnosis may require ruling out of the presence of a ruptured stomach or other serious injury. It takes only a few



Figure 9—Example of a ruptured diverticulum with an inflammatory mass surrounding it.

minutes to fluoroscope the patient and thereby be able to make a statement that *no air is present under the diaphragm.* Should the urine be bloody and there be a doubt concerning rupture of the kidney, intravenous urography will demonstrate, in 10 or 15 minutes, if there is a spilling out of the opaque medium into the perirenal structures thus indicating a rupture. The same films are of value in diagnosing any fracture of the pelvis, ribs or spine. Usually it is possible to make some statement regarding rupture of the urinary bladder at the same time, the return flow giving the indication.

IV. INFLAMMATION

In instances of *acute cholecystitis* or other acute lesions in which the gall bladder is the diseased abdominal viscus, Roentgen studies may be helpful in but a small proportion of selected cases. In general, the main contribution will be on a "flat film" or plain films of the area under suspicion, sometimes positively to diagnose a certain condition and again by negative findings to aid in differential diagnosis. The oral Graham test is contraindicated, especially when the patient already is vomiting or has fever; it is seldom used in urgent conditions. If however, the plain films show calcified gall stones or especially if the outline of an enlarged gall bladder is distinguishable, suggesting empyema of the gall bladder (Figure 10), the X-ray examination may be of great diagnostic value. Occasionally it happens that when a patient with an acute, abdominal condition is referred to the X-ray department for examination of the gall bladder, other lesions may be demonstrated unexpectedly, such as an obstructed small intestine, right renal stone, an enlarged pus-laden kidney, a sub-diaphragmatic abscess or even pyloric obstruction. Gaseous distention of the stomach and the intestines may aid the roentgenologist in correctly advising the proper examination to be carried out. Fluoroscopically, the appearance may be of value in detecting limitation of the excursion of the diaphragm due to a sub-diaphragmatic abscess or disease of adjacent viscera.

These remarks may not seem pertinent when a careful clinical diagnosis already has been made. Frequently, however, patients are referred to us for X-ray examination before a final clinical diagnosis has been arrived at and findings such as mentioned often aid the clinician more quickly to arrive at his diagnosis. *To the clinician, the value of the roentgenographic examination will depend largely upon the clinical alertness of the roentgenologist.*

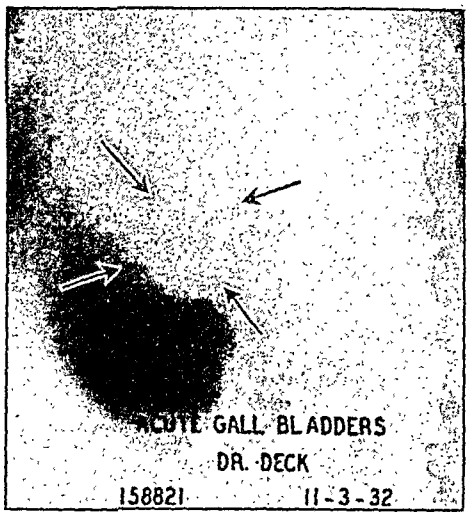


Figure 10—The patient was too ill to have performed a Graham test but this flat film of the abdomen made at the bedside demonstrates a greatly enlarged gallbladder shadow. At operation, the gallbladder was gangrenous, perforated and sealed in adhesions.

In the majority of cases in which the clinical diagnosis of *acute appendicitis* is made no one would think of having an X-ray examination made. In an occasional case, X-ray study may be necessary in order to rule out other lesions. For example, in children sometimes there is need for clinical

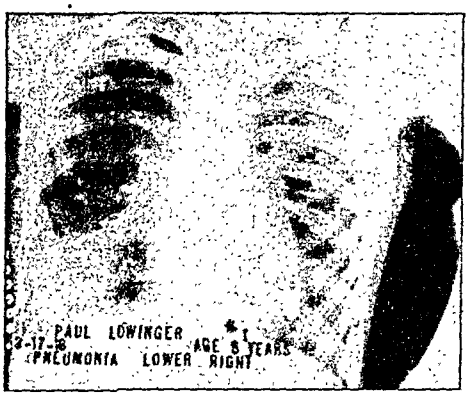


Figure 11—Child with lower right lobar pneumonia in whom the clinical picture was suspicious for acute appendicitis. The physical examination was indecisive.

differentiation between appendicitis, pneumonia of the right base or diaphragmatic pleurisy. (Figure 11). Bedside roentgen examination of the chest may prove a deciding factor in solving this problem since a pneumonic consolidation easily can be demonstrated. It has been stated that X-ray examination is not needed to establish the diagnosis of pneumonia: our experience has been that, except in rare cases, the X-ray will exhibit consolidation before physical examination can demonstrate it.

A second example of the utmost clinical value, is when it is necessary to rule out the presence of a urinary tract stone as the cause of symptoms in an instance where the affection may or may not be acute appendicitis. (Figure 12).

V. INTUSSUSCEPTION

Intussusception is quite commonly the cause of "acute abdomen," especially in infants. It is now well known that the

X-ray examination of patients in whom there arises suspicion of such a lesion offers considerable valuable information particularly to the surgeon.

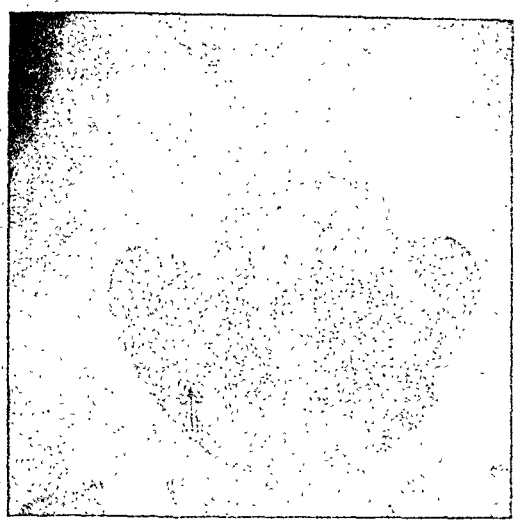


Figure 12—An example of a case with the clinical picture of acute appendicitis in whom the X-Ray examination demonstrated a urinary tract stone in the lower end of the right ureter.

Often, these patients are quite ill, but with patience and gentleness one can make X-ray examinations with the barium *clysma* without unduly delaying the operative procedure. In none of our cases has there been any ill effect from the opaque enema although most surgeons are fearful lest the



Figure 13—Example of how a barium *clysma* beautifully demonstrates the actual intussusception in the transverse colon.

barium may cause intestinal obstruction. The roentgenographic findings are almost pathognomonic in this lesion. In most cases, the upper segment of colon and a portion of the small intestines are invaginated into a lower segment of large bowel, resulting in such picture as is seen in Figure 13. (A section of the proximal colon is missing). At the point of invagination the infolding of the gut will be noted. Its border is irregular, the edge of the portion showing an indentation with dilatation. A tumor is present which, combined with the clinical symptoms of shock and of rectal hemorrhage, makes the diagnosis evident. (Figure 14).

VI. COLIC

Biliary colic often is the cause of "acute abdomen." Cases suspected of this lesion should be submitted to an X-ray examination as early as possible. There need be but slight disturbance to the comfort of the patient. Usually a "flat film" will give all the information possible. If the gall stone contains sufficient calcium, it can be recognized and the diagnosis established. It would be impossible to detect the stone should it lack adequate calcium content, unless the patient submits to a Graham test; seldom is that procedure justifiable.

One patient of an "acute abdomen" due to acute cholecystitis refused surgical intervention: the attack subsided and a Graham test then revealed gallstones. Later, during



Figure 14—A case of intussusception with dilated small intestinal coils present in the right mid-abdomen. Operation showed invagination of the terminal ileum, cecum and ascending colon.

another exacerbation of the ailment, the patient was operated upon and died.

Stones in the urinary tract usually contain sufficient calcium to be recognized on the "flat film." Certainly, all cases of "acute abdomen" where a urinary calculus is suspected should receive the benefit of an immediate roentgenographic examination. Non-opaque urinary stones must be thought of if the X-ray examination proves negative. As previously stated, intravenous pyelography can be done quickly; often it will demonstrate a uric acid stone which then is seen as a "negative shadow."

VII. HEMORRHAGE

The authors feel that usually, gross hemorrhage is a contraindication to X-ray examinations but this belief sometimes is over-ruled by a clinician who insists upon obtaining what information he can regarding the probable origin of the bleeding. It has been our experience that, with the patient who has previously been well and suddenly has a hemorrhage, the X-ray examination is of little value in localizing the bleeding point. If there is a history of previous indigestion or a diagnosis of ulcer, sometimes one is fortunate enough to demonstrate the lesion. As a rule, when there is only inflammatory reaction, bleeding is slight but is more or less constant. Massive hemorrhage oftener accompanies a malignant lesion or in ulcer, a duodenal rather than a gastric affection. In duodenal ulcer, the amount of inflammatory reaction around the lesion is not nearly so great as it is in a gastric ulcer; the blood vessels rupture more easily thus producing hemorrhage of large volume. These bleeding patients always are examined in the prone position and the examination thereby is limited in completeness. No compression films ever are taken until weeks after the patient's hemorrhage has ceased.

Finally, much more can be gained through cooperation between the clinician and the roentgenologist in their combined study of the diagnostic problems presented by instances of the "acute abdomen" than if each attempts, separately, to make differential diagnoses. The use of the X-ray in this often perplexing group of patients, bids fair to become of increasing value as the procedure is more extensively employed and pre-operative roentgen observations studied in the light of operative findings.

SECTION V—*Therapeutics*

CHRONIC ULCERATIVE COLITIS: TRENDS IN ITS PRESENT-DAY MANAGEMENT*

By

J. ARNOLD BARGEN, M.D.

ROCHESTER, MINNESOTA

A COMPREHENSIVE knowledge of the pathologic changes of chronic ulcerative colitis is essential if there is to be a clear understanding of the course which the treatment should take.

The lesion of this disease has its origin in the wall and not in the mucous membrane of the rectum and the colon. The evidence at hand points to a disease of systemic[3] origin, in which a streptococcus plays a dominant etiologic part. This microorganism and its toxin produce innumerable minute infarctions of the intestinal wall, with subsequent dissolution of intestinal mucosa.

This destructive process begins in the rectum and usually in that part of the rectum nearest to the anus. A condition which is defined as involving "the large intestine above the lower part of the rectum"[4] is not the subject of this paper, and that one observer apparently has based his opinions on cases in which the more proximal region was involved, whereas nearly all of the patients in our experience have had involvement of the more distal regions, may be the basis for some differences of opinion about etiology. In less than 5 per cent of a series of 1,472 cases (Table 1) encountered at The Mayo Clinic was there involvement of the large intestine

TABLE 1

Summary of eleven years' experience with chronic ulcerative colitis.

	1923	1924	1925	1926	1927	1928	1929	1930	1931	1932	1933	Total Cases
New patients.....	57	63	102	134	154	189	197	202	140	110	124	1,472
Cases in which ileostomy was performed.....	16	13	8	12	3	5	8	2	10	1	0	78
Postoperative deaths	7	5	6	5	3	2	6	1	5	0	0	40
Deaths among patients not operated on.....	7	6	6	9	4	4	6	6	2	3	1	54

above the lower part of the rectum if the lower part of the rectum was free from disease.

I shall consider a destructive infectious process, comparable in its devastating effect on the large intestine to that of tuberculosis on the lungs and hence demanding long-continued, careful, and well organized management (Table 1).

Before undertaking treatment, it is important to impart as accurately as is possible to the patient and his or her relatives, knowledge of this disease process.

Cases of chronic ulcerative colitis may be divided into two major groups from the standpoint of treatment: namely, (1) *the uncomplicated cases* and (2) *those in which there are complications* such as polyps, strictures, perforations, fistulae, regional disease and carcinoma. In cases in which these complications are present, (representing approximately 15 per cent of the whole), surgical intervention often is indicated.

I shall consider the uncomplicated cases and those in which systemic complications and sequelae are present, such as arthritis, erythema nodosum, uveitis, and other complications mentioned *infra*.

REST

Rest is an important therapeutic agent in these patients. The type of rest must be very carefully chosen. There is great need for encouragement, and for physical, mental, and physiologic rest. The features of treatment which the years have taught to be of value have not been discontinued, nor would it be expedient to replace them by a single therapeutic agent. In attempting to give rest to the intestine, the *residue in the food* is reduced as far as possible.

Intestinal irrigations usually are not only not helpful but, in the majority of cases, actually are harmful, causing more distress, greater frequency of rectal discharges, and often irritation about the anus. The only exceptions to this rule are to be found in the cases in which there is extensive ulceration of the anus and rectum, producing great local discomfort. In such cases, instillation or topical application of some soothing medicament or powder may be helpful.

At first, it might seem that the ideal method of giving rest to the colon would be by *ileostomy*. Actually, the risk of the operation is so great and the end results so disappointing that we at this Clinic avoid it as much as possible. In the seventy-eight cases in which ileostomy has been performed in a decade one of every two patients died in the hospital or later, and at the time of death had not recovered from the chronic ulcerative colitis (Table 1). Ten of the surviving patients, who were subjected to ileostomy for sequelae, after the colon practically had healed, were satisfied with the results.

IMMUNIZATION BY SERA, OR BY VACCINES

Immunization against the *diplostreptococcus* of chronic ulcerative colitis, with a concentrated serum, has been the most substantial part of our treatment for the last six years. The serum has been injected intramuscularly and, more recently intravenously. Injections are begun with minute doses; the dose gradually is increased and an attempt is made to keep the amounts given under the point of local or systemic reaction. *Improvement may be slow but usually is progressive.* Clearing up of the severe symptoms, such as fever, toxic states, and bleeding, may take weeks. As soon as this state is reached, treatment is continued with vaccine prepared from the *diplostreptococcus* of chronic ulcerative colitis. This vaccine may be given intracutaneously or subcutaneously, in increasing doses. The quantity injected is kept to less than the quantity which will cause local or systemic reaction for many weeks. After a period of rest of several months, treatment should be resumed and the vaccine given again for six or eight weeks.

*Division of Medicine, The Mayo Clinic.
Submitted for publication, April 20, 1934.

A program such as this should be continued for one or two years, or even longer, in some cases even if the patients are free from symptoms, to assure protection for the future. This procedure has proved the greatest single item in preventing recurrence of the disease.

TRANSFUSIONS

Transfusions of blood may have great value, particularly when the patient has bled profusely from the bowel, is very anemic and weak, or when marked sepsis, with high fever, prevails. A series of transfusions of small quantities of blood (250 to 300 c.c.), five or six days apart, possibly three in a series, has served best. Transfusions of as much as 500 cc.. are inadvisable.

Transfusions have proved particularly efficacious for children. Children less than twelve years of age, when affected with chronic ulcerative colitis, particularly are prone to the development of severe degrees of anemia.

DIET[1]

Many physicians undoubtedly restrict too greatly the *amount of food* allowed these patients and as a result the subjects lose in strength and in their ability to fight the infection. The ideal foods are those which are digested almost entirely in the small bowel and which thus leave very little residue for the colon. Some of the foods with the least residues are beef, rice, white bread, Italian pastes, sugar, well-cooked and strained cereals, cooked eggs, butter and cream. Every effort should be made to give these patients a diet sufficiently rich in calories so that the body weight can be maintained. When the patient is up and about the attempt is made to give a diet that will supply to the adult, approximately 3,000 calories.

Vitamins can be supplied in concentrated form, in fruit juices, yeast, butter, wheat germ, cod liver oil extract or irradiated ergosterol. A sample bland diet for patients with chronic ulcerative colitis is given in Table 2.

The foods in the "addition diet," supplementing the "foundation diet," will constitute a full diet, containing 80 gm. of protein and totalling 3,000 calories. Jelly or jam without seeds may be served, if desired. Beverages should not be iced. The patient is instructed to eat ice cream slowly. Condiments, such as mustard, horseradish, catsup, vinegar, and highly seasoned sauces or relishes, are best avoided. To lessen continued stimuli to peristalsis, food is not given between meals.

Contrary to the usual assumption, milk is not a low-residue food, and it is not well tolerated by many of the patients. It should, therefore, be used only with caution and in small amounts. Boiling the milk seems to make it only slightly more digestible. A number of writers, (particularly Larrimore), has considered that the good results sometimes seen when chronic ulcerative colitis patients are given enough food is due to the high vitamin content of the diet.

It can easily be seen that the *amount* and *quality* of the food given to these patients must vary largely with the severity of the disease. When the symptoms are acute, the patient may be able to take only a small amount of highly concentrated food. To patients in whom the affection is acute and fulminant it may be necessary for a time to give noting but liquids by mouth. To supplement oral feeding a solution of glucose may be injected intravenously and large amounts of physiologic saline solution injected under the skin. Not rarely, nourishment and fluid so administered enable desperately ill patients to weather crises.

TABLE II

Dietary regimen for patients with chronic ulcerative colitis.

"Foundation Diet" given on days 1 and 2*

BREAKFAST	DINNER	SUPPER
Cereal, †bland, 1 serving, with	Meat soup without vegetables, 1 serving	Steamed rice, 1 serving
Cream, ½ cup and sugar	Meat, 1 serving (liver three times a week)	Meat or fish, 1 serving or 2 eggs
Bacon, 2 strips	Potato, 1 medium sized, any way except fried	Bread, white or rye, 1 slice or equivalent amount of biscuit, zweibach, cracker, and so forth
Egg, 1	Gravy, if desired	
Toast, 1 slice	Bread, white or rye, 1 slice, or an equivalent amount of biscuit, zweibach, cracker and so forth	Butter, 2 squares
Butter, 2 squares		Bland dessert, ‡† no fruit, 1 serving
Coffee, if desired		Cream, 2 tablespoonfuls
Brewers' yeast‡	Butter, 2 squares	Tea, if desired
	Bland dessert,‡† no fruit, 1 serving	Sugar
	Cream, 2 tablespoonfuls	Brewers' yeast
	Tea, if desired	
	Sugar	
	Brewers' yeast	

The following foods may be added to the foundation diet as rapidly as the patient's condition permits:

"ADDITION DIET"

Order of Additions

Days 3 and 4—One banana, very ripe, and cod liver oil, 1 to 3 teaspoonfuls daily
Days 5 and 6—*Orange juice*, ¼ glass
Days 7 and 8—Vegetable puree, 2 tablespoonfuls
Days 9 and 10—Milk in the form of cream soup or milk toast
Days 11 and 12—*Whole milk*, 2 glasses
Days 13 and 14—Cream added to milk so that each of the 2 or 3 glasses taken contains half milk and half cream; bland fruit, canned or cooked peaches, apricots, pears, strained apple sauce, baked apple without skin, 1 serving
Days 15 and 16—Tomato juice, ½ glass or tomato jelly
Days 17 and 18—Whole cooked vegetable, 2 servings (puree, added on days 7 and 8, omitted) including, as desired, young tender carrots, beets, spinach, squash, peas, string beans, asparagus tips, potato any way except fried
Days 19 and 20—Shredded green lettuce cut very fine. Plain mayonnaise or cooked dressing may be used on the lettuce.

*Given on admission, contains approximately 60 gm. of protein and 2,000 calories.
†Cream of wheat, farina, puffed rice, puffed wheat, corn flakes, rice krispies and strained oatmeal.
‡Brewers' yeast, 200 mg. standardized vitamin fraction, is given with each meal.
‡†Custards, cornstarch puddings, junkets, gelatin desserts without nuts or fruit, plain rice puddings, simple cakes and cookies, cooked fruit whips, and plain ice cream

DRUGS

No single drug has been found which will help more than an occasional patient. Among the substances used may be mentioned iodine, gentian violet and arsenic. The former, in the form of fresh tincture, seems to have helped selected patients. Gentian violet in doses just sufficient to color the stools blue definitely inhibits growth of streptococci. Arsenic, in such preparations as treparsol, stovarsol, carbarsone or similar preparations, is dangerous. Since the recent widespread information about amebiasis, these drugs have been used somewhat indiscriminately. For chronic ulcerative colitis, arsenic should be used only as a last resort, because it may cause a flare-up of the disease. Once this has happened, it is very hard to do anything for the patient. The same from experience at this Clinic, can be said about mercury in the form of mercurochrome or metaphen.

Calcium and parathormone have been administered by some physicians where the affection has been mild. I venture to say, however, that in cases in which these drugs seem to have helped, the concentrated serum would have helped and would have given quicker response. Anemia, so commonly present in these cases, usually needs symptomatic aid and some form of iron is indicated. Administration of 3 to 4 gm. of reduced iron, daily, has proved helpful.

Camphorated tincture of opium and codeine often are helpful in patients in whom there are much pain and tenesmus, or in whom the stools are being evacuated so frequently that the subject becomes exhausted. Insoluble powders, such as bismuth, tribasic calcium phosphate and kaolin, occasionally are helpful.

REMOVAL OF FOCI OF INFECTION

All demonstrable or accessible foci of infection should be removed, if possible, because they may serve as depots from which reinfection of the bowel can take place. If one wishes to leave no stone unturned in the treatment of this disease,

one should remove teeth with periapical abscesses and with suspicious looking or definitely infected tonsils. Just *when* these procedures should be done must be dictated by the patient's progress and condition and the experience of his physician.

RELAPSES

The joy of the patient and the enthusiasm of his medical attendant at the successful treatment of this disease must always be tempered by the sober realization that the condition may recur. Knowledge of the pathologic changes which take place in this affection leads to wonderment, not that there *is* recurrence, but that healing *ever* takes place. Its close relation to disease of the upper part of the respiratory tract is again emphasized by the fact that 57 per cent of relapses were initiated by acute infections of the upper part of that tract.[2] Recurrences are more prone to occur during the winter months.

Much can be done to prevent relapses. Periodic use of the *diplostreptococcus* vaccine, removal of foci of infection, avoidance of extreme changes in weather and undue physical and emotional stress and strain, care in eating and drinking and preventing intestinal trauma, in its broadest sense, are only some of the many cautions which help to avoid exacerbations of a disease which is dreaded by those who have had it and which taxes the physician's ingenuity to the utmost during an attack, be it primary or recurrent.

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ABSTRACTS

RIVERS, ANDREW B., AND VANZANT, FRANCES R.
Mucin in the treatment of peptic ulcer associated with renal and hepatic disease. Annals of Internal Medicine, 7, 9, pp. 1122-1125.

It is here pointed out that although mucin treatment promised to circumvent some of the toxemic effects of alkalosis as produced by continued alkaline treatment in peptic ulcer, it has actually not accomplished this result. It was found in several cases that the administration of 60 grams of mucin three times a day brought about an elevation of blood urea to serious levels (72 mg. per 100 c.c.) and abetted renal and hepatic infections, associated with the cases. For this reason, although mucin may be safely used in uncomplicated cases of peptic ulcer, it should be used very cautiously where renal or hepatic complications exist.

F. L. T.

COLLENS, WILLIAM S., AND BOAS, LOUIS C.
Absorption of dextrose by rectum. Arch. Int. Med., 52:317-324, August, 1933.

Although dextrose does not pass through the membrane of the colon so rapidly as through the small intestine, a sufficient amount is absorbed to warrant recognition of this method as an acceptable therapeutic procedure. Experiments were performed in diabetic and non-diabetic patients who had no complicating rectal disorders. When the patient was in a fasting state in the morning, fourteen hours after a previous meal, a cleansing enema was first given, followed by an effective evacuation of the bowel. One hour after the enema, dextrose was instilled into the rectum in amounts which ranged from 20 to 100 Gm. in various concentrations. The dextrose was uniformly dissolved in distilled water. Blood examinations before and at varying intervals after instillation, as well as analysis of enema evacuation collected at the end of two hours, gave proof of absorption. The percentage of dextrose absorbed ranged from 59% to 91%.

B. S. C.

JOHNSTON, C. R. K.
Chronic Follicular Gastritis; G. S. & O., March 1934, LVIII, No. 3, pp. 614-619.

The author states that in recent years the more prevalent operation of gastric resection has made available valuable fresh material for study.

Stomachs, the site of chronic follicular gastritis, show a thickening and palpable stiffening of their walls in the pyloric region. Perigastric adhesions may be present; enlarged reddish lymph glands may be present above and below the pylorus. The mucosa is of a deeper pink color than normal and is covered with a thick, sticky mucous. The mucosal folds are often smoothed out, and tiny ulcerations or erosions may be present.

Microscopically the mucosa shows the most marked changes, which are localized to the pyloric region. The tubules of the gastric glands are separated by an infiltration of plasma cells and lymphocytes with varying numbers of eosinophiles in the deeper portions of the mucosa. In about one-half of the cases a marked hyperplasia of the lymphoid tissue, which may be aggregated into follicles with germinal centers, is seen. The presence of a number of these follicles warrants the diagnosis of "follicular gastritis." Marked atrophy of the mucosa with cyst formation is seen in advanced cases. If an acute process is superimposed, there will be a polymorphonuclear cell infiltration in the outer layers of the mucosa. The muscularis mucosa invariably is thickened or split into layers. The involvement of the sub-mucosa is common, but is much less pronounced. Islands of lymphocytes and eosinophiles are occasionally seen in the muscle layer and sub-serosa. Blood vessels in the sub-mucosa and sub-serosa are increased in number, and are distended.

In the author's series of thirty-seven cases diagnoses chronic follicular gastritis it was associated with duodenal ulcer on 18 occasions, with gastric ulcer on 8, gastric cancer on 3, and with stomal or jejunal ulcers in 4 cases. In 4 cases it existed alone. In one of these cases duodenal ulcer had been diagnosed and confirmed by X-ray. A second case was diagnosed and confirmed by X-ray as cancer, while neither carcinoma nor ulcer were found at operation. A third case was also diagnosed duodenal ulcer with doubtful X-ray finding; no ulcer was found at operation. In the fourth case the history suggested duodenal ulcer, but X-ray revealed only a polyposis of the duodenum; no ulcer was found at operation.

Of the 18 cases diagnosed in microscopical section as chronic gastritis duodenal ulcer was associated in 7, gastric ulcer in 4, gastric cancer in 3, and stomal ulcer once. The condition existed alone in 3 cases. In one of these the gastritis was very slight, the patient having swallowed a pin some days previously. Another case had been diagnosed as gastric ulcer by X-ray 6 weeks prior to operation, but no such lesion could be found. The third was associated with duodenal ileus.

In this series 37 of 56 surgical stomachs, by comparison with the normal stomachs obtained at autopsy, showed a definite inflammatory change in which marked lymphoid hyperplasia was a prominent feature. The definite localization of this change to the pyloric region has been interpreted as the expression of a special reaction of the mucous membrane in the region to a chronic peptic irritation. The etiology of this gastritis and its relation to the etiology of peptic ulcer, whether it be a primary lesion or merely secondary to the ulceration, has not definitely been established. The author is inclined to view the gastritis as a primary lesion, and believes that therein lies a fertile field for seeking the origin of the chronic peptic ulcer.

Nelson M. Percy.

SECTION VI—*Abdominal Surgery*

DIVERTICULOSIS AND DIVERTICULITIS OF THE SMALL INTESTINE

By

IRVIN ABELL*

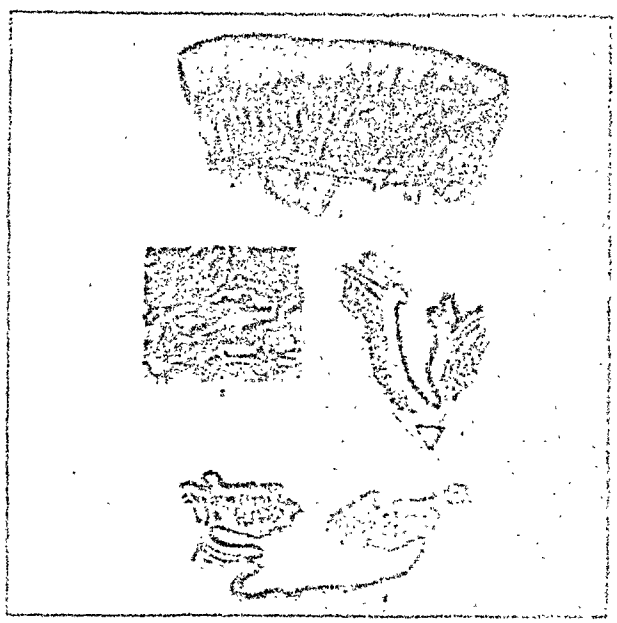
LOUISVILLE, KENTUCKY

DIVERTICULOSIS of the small intestine, first described by Chomel in 1710, has, with the exception of Meckel's diverticulum, received no surgical consideration until within the present century, most of which has been recorded in the past decade.

Diverticula are not infrequent in the duodenum, being found in all three of its divisions. They are less frequently observed in the upper portion of the jejunum and with the exception of the diverticulum of Meckel but rarely seen in the ileum. In the majority of the reported cases the opening into the sac has been situated on the mesenteric side while both lateral and ante-mesenteric openings have been described. Both the congenital or true and the acquired or false types are found in the small intestine and are observed at all ages, the latter being most frequent at and after middle age. The former have been found in infants at birth and are usually single; they have been found with pancreatic tissue at their apices, while their most frequent location in the duodenum is near the papilla of Vater, where the pancreatic ducts are developed from duodenal buds. The acquired type develops and produces symptoms late in life when atrophy of the muscularis, particularly of the circular coat, may be a predisposing factor and occur most frequently on the mesenteric side of the bowel where the vessels penetrate the muscularis. They vary in depth from ⅛ of an inch to 2 inches or more. The fluidity of the contents of the small intestine is such that solid material is rarely found within them although the *stomata* which connect the diverticula with the intestine are smaller than the cavities of the diverticula. Chomel 1710, Harley 1875, and Cole and Roberts (1920) have reported diverticula of the duodenum containing gall stones while Terry and Mugler and C. M. Watson report instances of intestinal obstruction due to the formation of enteroliths in diverticula of the jejunum. Morrison and Feldman report a primary carcinoma in a duodenal diverticulum. Diverticulosis of the small intestine may exist throughout life without giving rise to symptoms, being found only at autopsy. With the retention of decomposing food leading to distension, irritation and inflammation of the sac or its surrounding structures, symptoms arise. None of these is pathognomonic and a diagnosis cannot be made on clinical evidence alone.

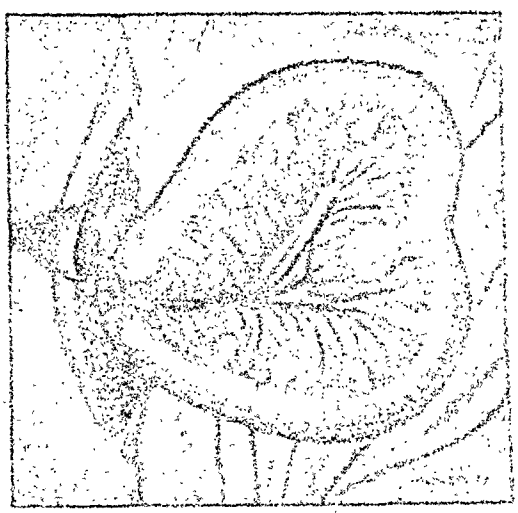


1. Multiple Diverticula of the Jejunum. Sheppe.



2. Jejunal Diverticula. Helvestine.

Diverticula are not infrequently associated with peptic ulcer, cholecystitis and pancreatitis and when so the symptoms caused by the latter will predominate or else becloud the picture.



3. Diverticula of Jejunum with fecolith producing partial obstruction. C. M. Watson.

*Clinical Professor of Surgery, School of Medicine, University of Louisville.

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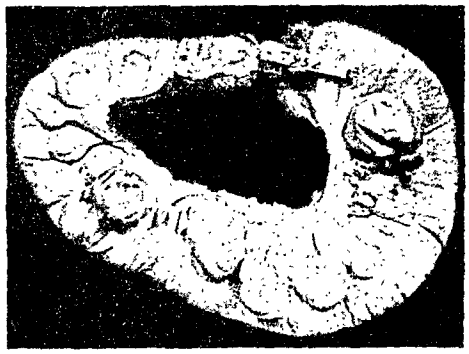
Clinical Picture: Upper abdominal discomfort varying from a slight ache to severe colicky pain is one of the commonest symptoms. The pain may be relieved by food or alkali or may recur after eating and there are frequently long periods of freedom. Sour stomach, belching and nausea are at times noted. The symptoms are so indefinite and so variable, simulating those of lesions of adjacent organs, that clinical deduction alone will not permit a diagnosis. They may, however, be demonstrated with a high degree of accuracy with the X-ray. The information which such an examination



4. Diverticulum of Duodenum.

affords gives one an important lead in evaluating the significance of the presence of diverticula.

Basis for Type of Therapy: Those which are discovered accidently during routine X-ray examination of the gastro-intestinal tract and which are not causing symptoms require no treatment. Those in which inflammatory changes are present may require excision. The observation of retention of barium in a diverticulum for a much longer time than is required for the emptying of the stomach, associated with tenderness on point pressure, when other upper abdominal lesions are ruled out, may be considered as indicating diverticulitis. In the event of associated ulcer, cholecystitis or pancreatitis, it becomes a matter of judgment in correctly appraising the role played by each and determining for or against excision of the diverticulum in addition to the appropriate treatment of the associated lesion. In case of doubt or in debilitated patients in whom the excision would materially enhance the operative risk, the latter procedure may be



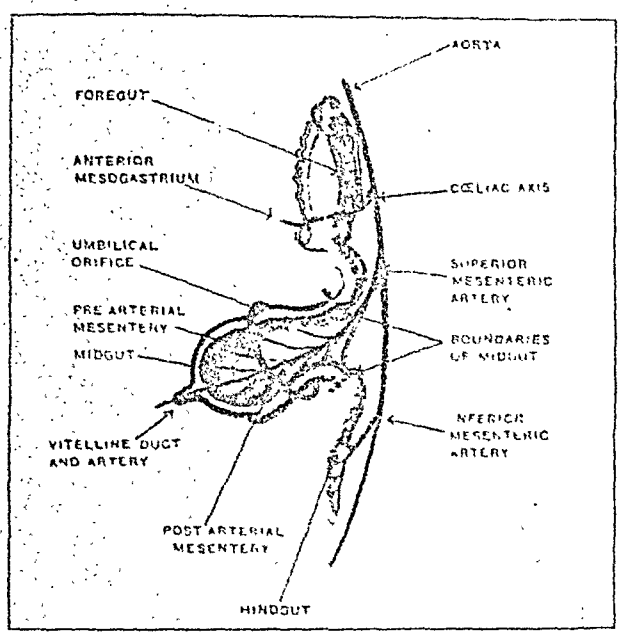
5. Diverticula of Jejunum. W. D. Gatch.

omitted until such time as the indication for it becomes more apparent. In patients in whom the employment of surgery is contraindicated and in those in whom symptoms are not sufficiently definite to warrant operation, a medical treatment based on that for duodenal ulcer is most likely to give good results. When the roentgenological examination has shown the presence of spasm of the pylorus or duodenum the additional employment of belladonna will be helpful. Constipation, which is a frequent accompaniment, should be relieved by appropriate measures. The complications of diverticulosis of the small intestine which demand surgery for relief are diverticulitis, suppurative peridiverticulitis, perforation and intestinal obstruction. The important anatomical points to be borne in mind are the relation of the peritoneum to the sac, the relation of the sac to the vascular supply of the intestine and the relation of the sac to adjacent structures. The latter point is particularly applicable to duodenal diverticula which may be in close relation to the common duct, in front of the pancreas, behind the pancreas or buried in its head. The surgical procedure employed must be suited to the pathology found: invagination or excision of the sac with closure of the defect in the intestinal wall, fortifying the latter where possible with an omental fat graft; drainage of abscesses with or without excision of sac; resection of intestine or pylorus; gastro-enterostomy, all find a place in the various pathological pictures presented.

Diverticula of the Ileum: The most commonly observed diverticulum of the ileum is the persistent intra-abdominal portion of the vitelline duct, first accurately described by Johann Friedrich Meckel and given his name, since 1912. The vitelline or omphalo-mesenteric duct connects the yolk sac with the midgut and normally becomes obliterated from the seventh to the eighth week of fetal life, the atrophy beginning at the distal end and progressing usually until the lumen of the ileum is reached. The artery and veins which accompany this duct normally disappear entirely except that portion which becomes the superior mesenteric artery and vein. Complete failure of obliteration will leave a tube communicating with the ileum at one end and with the umbilicus at the other, from the latter of which feces are discharged. Obliteration at both ends will leave a tube connected by a fibrous cord either to the umbilicus or the ileum or to both. Such a remnant may give rise to tumors of various types, cysts, carcinoma, sarcoma and malignant myoma having been reported. Obliteration at the distal end leaves a tube of varying length connected with the ileum and communicating with its cavity. It may be found at any point of the small intestine below the duodenum, the usual location being from ten to thirty inches above the ileo-caecal opening. Its usual attachment is antemesenteric and its length varies from a small protrusion to one reported by Moll thirty-three and one-half inches long. Its distal end may be free or be attached by a fibrous band to the umbilicus, mesentery or adjacent organ. In shape it may be spherical, conical, bulbous or somewhat like the finger of a glove. Its walls consist of the normal coats of the ileum, possessing at times Lieberkuhn's follicles, Pyer's patches, gastric mucosa and even accessory pancreatic tissue.

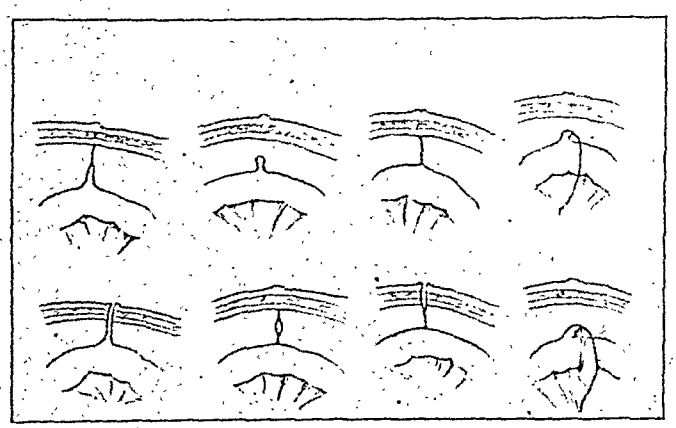
Its incidence as estimated from autopsy statistics varies from one to two percent. Surgical records have shown a varying incidence, as a rule somewhat lower than that derived from post mortem studies. This interesting vestigial remnant is responsible for a number of acute abdominal conditions which carry a potentially high mortality. It is a prolific cause of intestinal obstruction as a result of its attachment to the umbilicus or to some other portion of the parietal peritoneum, mesentery or intestine, resulting in constriction by band or kinking from traction. Volvulus of the diverticulum itself has been reported as well as of the loop of ileum from which it springs. Obstruction may be produced by an intussusception, the intussusceptum having for its apex the invaginated diverticulum or the point of the ileum from which it arises. Hertzler and Gibson in 1913 reported such a case together with a careful study of 41 similar instances recorded in the literature. The average age was 13 years with 49 percent under 10 years of age. Of the 22 resections in the series 13 died and 9 recovered, a mortality of nearly 60 percent. Further reports are available in the literature; but

recently we have observed this complication in a boy of 6 years, admitted to the hospital moribund with a palpable mass in right lower quadrant. A diagnosis of intestinal obstruction due to intussusception was made from the history and physical findings. Autopsy showed an invaginated diverticulum with the ileum telescoped into the ascending colon. Inflammation of Meckel's diverticulum mimics very



6. Embryology of Intestine. Ochsner.

closely that observed in the appendix, both as regards the symptoms and the sequence of pathological events dependent upon it, causing diverticulitis, peri-diverticulitis, abscess and perforative peritonitis. The symptoms of obstruction produced by the various lesions of Meckel's diverticulum as well as those of the inflammatory phenomena induced by it do not in any wise differ from those arising from other causes. The history of a persistent umbilical fistula or the finding of an ileo-colic intussusception in a subject beyond the age of infancy is suggestive as are right sided appendiceal symptoms in the known absence of the appendix. X-ray studies have

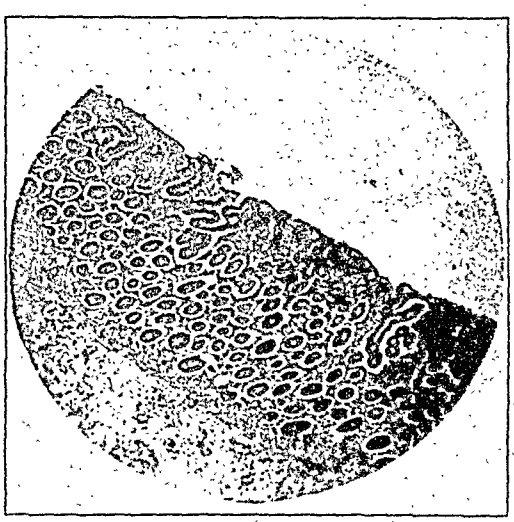


7. Possibilities of Meckel's Diverticulum. Hudson.

been of little value in the recognition of its presence. No one symptom or combination of symptoms, aside from the presence of a congenital umbilical fistula, can lead to any high percentage of correct diagnoses. The important lessons to be learned from the literature of Meckel's diverticulum are that its complications possess an inherently high mortality and an appreciation of the significance of prompt diagnosis, at least, of an abdominal emergency, with consequent early operation.

The procedures employed must needs suit the individual case and consist in enterostomy, release of obstructive bands and intussusception, ablation of diverticulum, resection of intestine and drainage as indicated by the pathology found. In view of the possible dangers from a Meckel's diverticulum, it should be removed when encountered in the course of operations for other lesions. My associate and I have seen symptomless diverticula in 31 instances, 30 in the abdomen and one in the sac of an inguinal hernia. Twenty-nine were removed; the remaining two possessed such wide openings and shallow depths as to render improbable the occurrence of complications.

Shaetz in 1923 pointed out that islands of gastric mucosa occur in the vitelline duct and proposed the theory of embryonal transplantation. Later he studied thirty specimens of Meckel's diverticulum by serial section. Of these only 17 or 57 percent were free of abdominal elements. Three, or 10 percent, showed mucosa belonging to higher segments of the small gut, jejunum and duodenum. Five, or 16.6 percent, presented islands of gastric mucosa; one contained pancreatic tissue and one pancreatic tissue and gastric mucosa. Meulengracht in 1918. Magerand and Durant in 1922, Ciubal, and Hollopean and Humbert in 1924 reported instances of peptic ulcer in Meckel's diverticulum showing both hemorrhage and perforation. Ascher and Karelitz in 1930 collected and studied 33 reported cases of peptic ulcer in Meckel's diverticulum and the ileum. The most common symptom was the passage



8. Aberrant gastric mucosa in Meckel's Diverticulum. Jackson.

of fresh blood and clots per rectum; it was absent in but five of the 33 cases and in one of these anemia was noted. The periods of bleeding varied from one of thirty-six hours duration causing death in an infant, to a man of 28 who had repeated hemorrhages since childhood. Pain of some sort was noted in 21 cases, in many its onset being coincident with perforation. Sudden perforation was noted in eleven, one-third of the total number. A palpable mass was observed in three: this with the passage of blood suggested intussusception, but the stools lacked the usual admixture of mucus and the symptoms of obstruction were wanting. Gastro-intestinal X-ray studies were made in six cases without giving helpful information. They suggest that unexplained cases of repeated intestinal hemorrhages, in which other lesions, have been excluded, be subjected to exploratory laparotomy: if peptic ulcer or Meckel's diverticulum be found, the operation of choice is excision of the diverticulum with enterorrhaphy at right angles to the long axis of the intestine. Their summary is as follows: "Heterotopic gastric mucosa has been shown to occur at the umbilicus as a result of anomalous developmental structures arising from the omphalo-mesenteric duct. Such areas of mucosa have been demonstrated to produce a secretion containing free hydrochloric acid and pepsin with irritation, erosion and ulceration of the surrounding skin. The secretion could be excited by the ingestion of food or by local mechanical stimili. Heterotopic gastric mucosa has also been demonstrated in Meckel's diverticula which have retained

their connection with the lumen of the ileum. Chronic ulcers causing pain, hemorrhage and perforation, and histologically identical with peptic ulcer of the stomach, duodenum and jejunum have been described in Meckel's diverticulum and the ileum in thirty-three cases. In twenty-one of these, gastric mucosa was demonstrated in the diverticulum. The ulcers occurred in the intestinal type of mucosa adjoining the heterotopic gastric mucosa, being frequently located at the neck of the diverticulum which was usually completely lined by gastric mucosa."

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THE CONGENITAL PERICOLIC MEMBRANE SYNDROME, OFTEN MISNAMED CHRONIC APPENDICITIS*

A PRELIMINARY REPORT OF OBSERVATIONS

By

W. H. BUEERMANN, M.D., Ph.D.

PORTLAND, OREGON

ASTUTE clinicians and surgeons long have had misgivings regarding the accuracy of diagnosis when dealing with patients presenting a chronic symptomatology referrable to the right side of the abdomen. This hesitancy to venture a definite diagnosis frequently has resulted in a compromised opinion especially when the usual laboratory aids of blood studies, stool examinations, and roentgen films have given no positive findings which would classify the disturbance under any of the definitely known clinical syndromes.

Chronic cholecystitis without lithiasis, chronic appendicitis and chronic colitis have often been given as compromise opinions upon which medical and surgical procedures might be based. A gall bladder or an appendix is removed, a diagnosis of chronic cholecystitis or chronic appendicitis is rendered by the pathologist but the patient continues to complain of the same symptoms presented prior to operation, and in precisely the same location with possibly minor variations in the clinical picture.

Obviously then, the removal of the pathologic evidences of chronic inflammation have not relieved the subject and discouragement follows to patient and physician alike.

An analysis of the histories of many of these unrelieved patients later may reveal the fact that other well-known causes capable of producing right-sided abdominal symptomatology had not been accurately excluded. A carefully taken history will, on many occasions, reveal the clue to the overlooked syndrome. Inflammatory, neoplastic, and obstructive lesions of the right kidney, right urogenital structures, right half of the colon and lower ileum and the liver must be considered. Inflammatory and neoplastic lesions of the vertebrae involving the spinal nerves supplying the right abdominal region must not be overlooked in the more obscure types of disturbances. Even after all of these possibilities have been considered there still may have been present a group of symptoms which has eluded the grasp of clinical investigation and too often has led to the enigmatic terminology of neurosis, or abdominal neurasthenia. The frequent association of the "neurasthenic" individual and right-sided symptomatology has been observed by many clinicians; the attempt to relieve this group of individuals by a diagnosis of chronic appendicitis or of chronic cholecystitis followed by the removal of these structures only, as mentioned, has failed to bring the anticipated relief.

The patients presenting themselves with the symptom-complex we have generously regarded as signifying the presence of chronic appendicitis, are, in many instances prevented from following their occupational pursuits; after removal of their appendices only, still complain bitterly of a continuation of the same symptoms and disability which caused them to submit to surgical procedures in the hope of finding relief, even when all seemingly-known differential possibilities previously had been excluded.

It follows, then, that there must be still another syndrome, or symptom-complex, which has not been clearly elucidated as a clinical entity. If this be so, then its application to this group of unfortunates should bring to our differential diagnostic consideration another group of symptoms which should be diagnostic for such a condition *prior* to surgical intervention.

The author's interest in such a possible syndrome dates back about five years. The inception of the interest was due to a natural self-blame for not having relieved a patient suffering from "chronic appendicitis" by removal of the appendix only, although, at the time, pericolic membranes were seen to be present but were considered as of no consequence in the production of the patient's symptomatology.

However, a review of the literature upon this subject awakened a desire to determine if possible the presence of a syndrome which might make it possible to diagnostically differentiate those symptoms produced by membranous interference with the normal activities and functions of the right half of the colon and lower ileum from these due to appendiceal inflammation alone, whether subacute or chronic in nature.

HISTORICAL CONSIDERATION

The early work of Soemmering,[1] Virchow,[2], Toldt,[3], Treves,[4] Jonnesco[5] and Juvara and others from the standpoint of pathologic anatomy of the colon did much to stir early interest in the developmental defects found in the normal and abnormal attachments of the right half of the colon and lower ileum.

With the decade preceding the turn of the century, the association of the syndrome of appendicitis with disturbances in the right lower quadrant became an accepted entity. If

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the symptoms in the region of the appendix were unassociated with acute illness, a diagnosis of chronic appendicitis was considered. If associated with acute symptoms, acute appendicitis was the generally accepted diagnosis. Any membranes found in the region of the ascending colon and cecum were considered to be the result of chronic appendiceal inflammation.

Riedel,[6, 7, 8, 9] Lauenstein,[10] Hochenegg,[11] Haberer[12] and Lane during this period described and reported cases of so-called chronic appendicitis associated with omental, gall bladder, appendiceal, colonic and ileal membranes and bands, in which cases, colicky, right-sided, abdominal pain and other symptoms of partial obstruction of the bowel were manifest. Removal of the appendix only, in the presence of constricting membranes of the right half of the colon, was found to mean a persistance of the major symptoms.

Lane,[13] in 1903, discussed the membranes supporting the ascending colon and stated in several papers that these membranes frequently produced interference with the free passage of intestinal contents through the hepatic flexure. He called this membrane "a false mesentery" extending from the ascending colon and hepatic flexure to the posterior abdominal wall lateral to the kidney. He believed that the primary factor in the production of inflammation of the appendix was obstruction of the hepatic flexure and that trouble in the appendix was a secondary manifestation. He stated further that, "many of the patients complaining of pain in the right iliac region are not appendiceal at all but are the result of chronic obstruction of the caecum and ascending colon, and the removal of the appendix is in itself unnecessary and a luxury." His later work on chronic constipation and intestinal toxemia, together with an unusually radical surgical approach to this problem, divorced the attention of the profession from the salient, basic facts which Lane first presented.

Wilms[14] and Jackson,[15] in the first decade of this century, did much again to call attention to the futility of expecting a clinical cure in patients complaining of pain in the right iliac fossa by a simple appendicectomy, when there were present congenital membranes constricting the ascending colon and the hepatic flexure.

Harvey,[16] in 1918, presented an excellent review of the literature and pointed out the *various types of congenital membranes encountered in the right half of the abdomen.* The reader is referred to this work and to the work of Taylor[17] for a comprehensive review of the known clinical factors involved in the problem of congenital, pericolic membranes.

Rea Smith[18] and Bigelow[19] have presented more recent clinical studies of chronic appendicitis and congenital pericolic membranes and have recorded clinical results obtained in this group by surgery directed towards the pericolic membranes as well as towards the appendix in so-called "chronic appendicitis."

In none of the preceding clinical discussions, however, has there been mention of a *clinical syndrome arising from the presence of these congenital membranes*, which syndrome might be utilized to diagnose or suspect their presence, since it has been assumed that the syndrome called "chronic appendicitis," (even though it remained unrelieved by appendicectomy) sufficed, clinically.

THE CONGENITAL MEMBRANES

This discussion, being a preliminary presentation of complete clinical observations to be published later, will not enter into a discussion of the embryology nor present the detailed description of all the membranes encountered in the right half of the abdomen. However, the following outline exhibits the more frequent groups encountered, without attempting a detailed description.

TYPES OF MEMBRANE ENCOUNTERED—

I *Cysto-colic Group* of membranes and ligaments:
- 1—Gastro-hepatic ligament, Harris.
- 2—Hepato-duodenal ligament, Harris.
- 3—Hepato-colic fold, Luschka.
- 4—Cysto-colic fold, Luschka.

II *Hepatic Flexure* Membranes:
- 1—Reno-colic ligament of Haller.
- 2—Lane's "false" mesentery.

III *Ascending Colon* Membranes:
- 1—Mesenterico-colic folds.
- 2—Parieto-colic fold of Jonnesco and Juvara.
- 3—Jackson's "membrane."
- 4—Lane's "false" mesentery.

IV *Pericecal* Membranes:
- 1—Blood-less fold of Treves.
- 2—Parieto-colic folds (external and internal).
- 3—Mesenterico-parietal fold.

V *Lower ileal* folds and membranes:
- 1—Ileo-pelvic band of Treves and Lane.
- 2—Genito-mesenteric fold of Reid.
- 3—*Plica genito-enterica* of Treitz.

Some of the subdivisions mentioned above are synonymous for the same membrane, band or fold described by different authors.

CLINICAL PHASES

The clinical symptoms and signs of acute appendicitis and acute recurring appendicitis, with all symptoms and signs referrable to McBurney's point and with laboratory data in agreement, will not be discussed here since there is, in the majority of cases, slight differences of opinion as to the diagnosis of this group clinically.

The diagnosis of the so-called case of "chronic appendicitis" is not so readily accepted.

Most text books treat this subject as though it were a definite clinical entity, whose only interest to the clinician, provided it remains *chronic*, is the symptomatology reflexly produced. The question has been raised as to whether this clinical picture has any standing in clinical surgery as such. It is not within the province of this paper to discuss the contraversorial factors of this condition other than to emphasize the symptom-complex so frequently described in the literature as considered due to chronic, inflammatory disease of the appendix. These symptoms and signs are, occasional nausea and emesis, eructations, a sense of fullness after meals, occasional slight rigidity of the right rectus muscle, tenderness over McBurney's and Morris' points, meteorism at the cecum (balloon sign), Rovsing's gas-pressure-pain symptom, sex-gland pain and pain in the supposed region of the appendix produced by activity.

It is true that fecolith formation in the lumen of the appendix with poor drainage, and a retrocecal appendix with kinking of the appendix lumen frequently will give rise to some of the above symptoms. A preceding "acute attack" has at times been considered a necessary prerequisite to a diagnosis of "chronic" appendicitis.

However, in any event, if the true origin of the patient's chronic right-sided symptoms resided in the appendix alone, them *appendicectomy alone* should bring about a cure of the patient's condition and, *irrespective of the pathologist's findings*, a diagnosis of chronic appendicitis might be considered as valid.

CONGENITAL PERICOLIC MEMBRANE SYNDROME

As a result of the past five years' observations, covering a series of 72 patients, to be reported in detail later, five clinical "axioms" have become established, which "axioms" the author requires to be substantiated in the given case, before one may assume that a clinical entity, due to the presence of harm-producing pericolic membranes and bands, exists. It is assumed in this discussion that the usual differential diagnostic factors properly have been ruled out:

1. There must be a definite anatomic basis in or about the right half of the colon to produce the symptomatology which persists unrelieved after appendicectomy for so-called "chronic appendicitis." If anatomic in nature, there must be an abnormal situation present, such as constriction or rotation, in order to produce an altered physiology of the functions of the colon. This we believe can be demonstrated.

2. If the syndromes of so-called "chronic appendicitis" and congenital pericolic membranes and bands overlaps, then, when the appendix only has been removed, we should still have remaining the syndrome arising from the presence of constricting, congenital pericolic membranes, as a relatively pure clinical syndrome. This we believe we have been able to demonstrate.

3. If the syndrome arising from the presence of constricting pericolic membranes still is present after appendicectomy; then a correction of the causative factor producing this anatomic defect, *i.e.*, by adequately sectioning the constricting membranes and bands, should relieve the patient of the symptoms unrelieved by appendicectomy alone. This we have *demonstrated clinically*. (See also the work of Rea Smith and of Bigelow.)

4. If the symptoms and signs considered as indicative of the presence of congenital pericolic membranes can be classed as a "syndrome," then we should be able to identify it as such in all age-groups, beginning with infancy in some instances, in children as early as two to three years of age and in the various age groups found in grade-schools, high-schools and colleges. The syndrome also should be found in adults of all ages with a preceding history of recurring disturbances conveying a clinical pattern similar to the one considered as indicative of the presence of congenital pericolic membranes. We believe that this fact has been demonstrated in our clinical experience. The diagnosis has been made pre-operatively and proven surgically in age-groups ranging from three years to fifty-five years. It has been recognized in a patient of sixty-six years and the same "clinical pattern" traced back to early youth.

5. If abnormal attachments of pericolic membranes are congenital in nature, then, in a reasonable number of patients, one should be able to demonstrate familial or hereditary tendencies, i.e., the same identical syndrome as outlined below should occur in parent and child in a certain percentage of subjects. Since this aspect has been recognized, identical, pericolic-membrane-syndromes have been found in the familial studies. A number of instances of father-and-son, and mother-and-daughter similarities have been analyzed. In none of these instances, had the similarity been recognized until the symptom-complex mentioned below had been outlined. The "exercise-symptom" relationship then became very apparent only in those definitely affected, even to non-relief by appendicectomy.

UNDERLYING BASES FOR SYMPTOMS AND SIGNS

If we assume that a definite clinical symptomatology can be based upon the presence of constricting, congenital pericolic membranes and folds, this symptom-complex should then be explainable on the following basis:

1. There should be a group of symptoms arising from the physical presence of these membranes, bands or folds which are producing the constriction. At times, there should be symptoms arising from within the sensitive peritoneum covering these membranes or from the tension and tugging upon the membranes at either their parietal or the visceral attachments, especially when they are inflamed.

2. There should be local and systemic symptoms secondary to partial and intermittent obstruction of the bowel-lumen (ileum, or right half of colon) by these congenital bands, folds or membranes. These obstructive phenomena may arise from either a constriction of the bowel-lumen by bands or membranes, or from rotation of the bowel on its normal axis by the membrane attachments with resultant torsion, and decrease in bowel lumen.

3. There should be reflex symptoms and signs arising from the gastro-intestinal tract proximal and distal to the point of constriction or mechanical interference by these membranes, i.e., an altered physiology of the nervous control and the digestive function of the gastro-intestinal tract.

SYMPTOMS AND SIGNS OF THE "PERICOLIC-MEMBRANE-SYNDROME"

In a discussion of the following symptoms observed under the three classifications mentioned, the grouping does not necessarily mean that in *each patient* all of the following symptoms will occur. However, when the presence of congenital pericolic membranes is suspected from the history, many of the following symptoms and signs may be elicited from the patient by a well taken history and a painstaking physical examination, in which the following factors adequately are evaluated.

SYMPTOMS AND SIGNS DUE TO THE PHYSICAL PRESENCE OF CONGENITAL PERICOLIC MEMBRANES

1. A sensation of pain, aching or soreness along the right infra-costal border extending *posteriorly* along the level of the 11th and 12th ribs laterally and posteriorly. This is especially noticeable after excerise or during an attack of right-sided colic. This soreness may extend inferiorly along the lateral border of the ascending colon, the area usually represented by the constricting membrane. (Figure 1.).

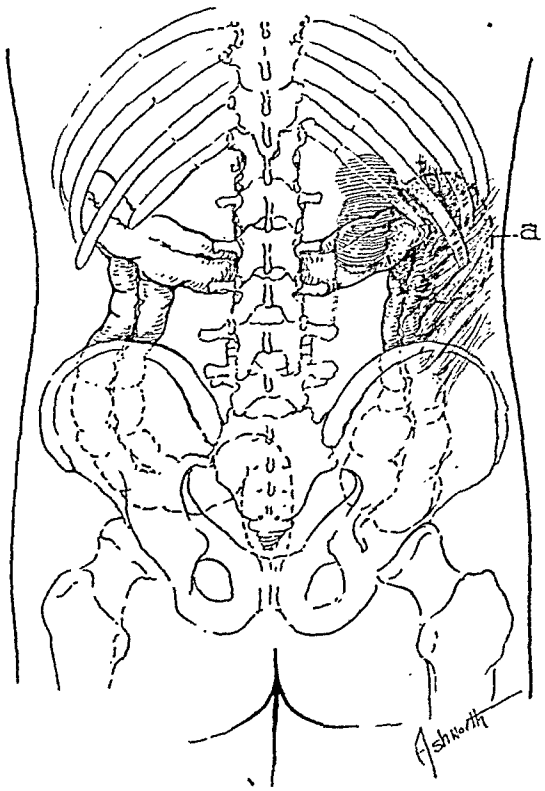


Figure 1—Sketch showing relationship of right kidney to hepatic flexure of colon. (a) represents zone of tenderness and pain arising from postero-lateral attachment of parieto-colic membrane.

POSTERIOR VIEW

2. Tenderness over the region of the 10th rib posteriorly on the right side, especially during and immediately following an attack, the tenderness frequently simulating right kidney involvement, even though the kidney may have been proven to be free from pathologic changes.

3. Hyperaesthesia in the right flank, over the 10th rib posteriorly, frequently is noticed, especially *following exercise* or *during an attack* of right-sided discomfort.

4. A positive kidney punch sign has been found present over the posterior and anterior attachments of the congenital

pericolic membranes, in the absence of temperature or signs of infection. This is particularly noticeable during periods when the membranes have been irritated by constant cough, hyperperistalsis from laxatives or after exercise. A perinephritic inflammation has been suspected on several occasions during such periods of tenderness, without rise in temperature, induced by the renal capsular attachment of a reno-colic membrane.

5. A feeling of soreness, a sense of pulling or of painful "drag" along the lateral border of the ascending colon and hepatic flexure when lying on the left side at night—"drag sign." (Figure 2).

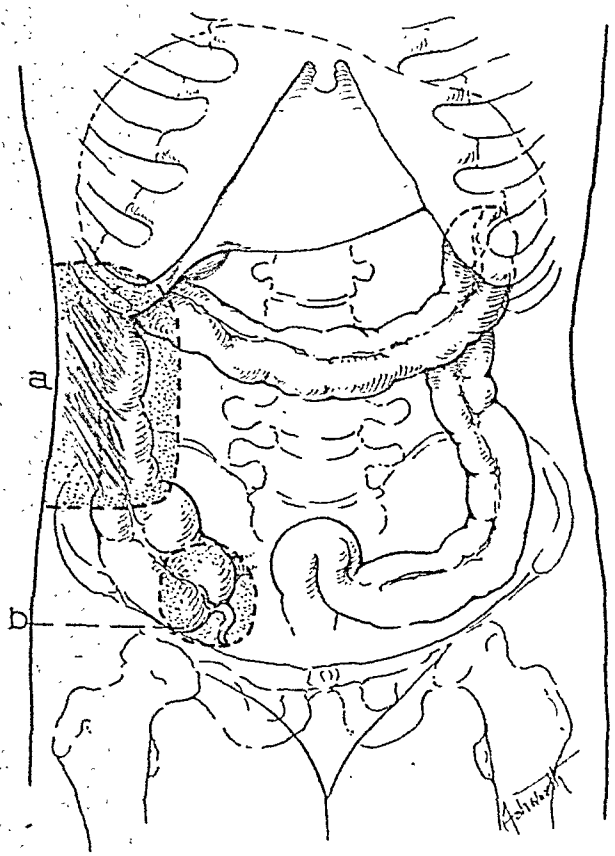


Figure 2—Sketch showing torsion of ascending colon with dilated cecum produced by parieto-colic membranes along ascending colon. (a) area of pain and drag during exercise. (b) zone of tenderness in region of appendix and ileo-cecal valve.

6. Pain in the upper, right flank anteriorly, under the inferior lateral border of the liver, especially when the right arm is raised over the head. This symptom will be most frequently exaggerated in occupations where the frequent elevation of the right arm over the head is required.

7. Pain or tenderness along the lateral border of the colon or the hepatic flexure may be elicited during or subsequent to an attack of right-sided colic, by manually slowly drawing the bowel towards the mid-line with the examining hand. This exerts a slight "drag" upon the membranes, and, when inflamed, will give rise to the same sensation of discomfort which is experienced by the patient during or subsequent to exercise.

8. There is, occasionally, a complaint of pain in the upper right flank induced by repeated coughing or emesis. This has, upon three occasions noted by the author, been called pleurisy, without evidence of temperature and without evidence of pleural "rub" and with a designated location pointing to the hepatic flexure of the colon and too low for the pleura. In each case, an enema, with sufficient fluid produced immediate relief of the "pleurisy" upon the passage of a hard, constipated stool.

9. After appendicectomy for chronic appendicitis, many of these symptoms referrable to the lateral aspect of the ascending colon, caecum and hepatic flexure still are present as a congenital pericolic membrane "tug" or "drag."

10. Pain in the right flank may be replaced by a feeling of ache or fatigue in the right flank and right lumbar areas at the level of the 10th rib posteriorly, especially after periods of physical activity or after train, automobile or trolley rides.

11. There is a definite relationship between the recurring attacks of soreness in the right flank and exercise or activity in the presence of congenital pericolic membranes. Activities such as running, jumping, long automobile rides, lifting, swinging from gymnasium bars or rings, basket-ball, horse back riding, aesthetic dancing, golf and hiking have been found to induce soreness and tenderness along the parietal and visceral attachments of the pericolic membranes. This is then later associated with right-sided colic, nausea and vomiting and tenderness over the cecum. It is in this period that many of these patients first are seen and the preceding activities entirely disconnected from any etiological connection. A normal leucocytosis and normal temperature associated with right lower quadrant pain, associated with colicky pain, nausea and vomiting send many of these patients to the hospital for observation, only to be sent home again the following day after the laboratory findings have been reported as normal.

12. There is, not infrequently, an associated right ovarian and right pelvic pain associated with pain in the right flank. this is frequently caused by the "ileo-pelvic band of Lane" or the "genito-mesenteric fold of Reid" which the author has been able to demonstrate in two cases of genital-gland pain in women.

13. Relief from the "drag-sign" is obtained by the patient's being able to lie on the right side in perfect comfort, whereas, distress and aching are produced in the right flank when lying on the left side in the presence of inflamed congenital pericolic membranes and folds causing ascending colon and hepatic flexure constriction.

LOCAL SYMPTOMS AND SIGNS

1. There are recurring attacks of pain and colic noticed in the region of the cecum and ascending colon, especially after a period of exercise. These attacks are frequently present at night when the patient relaxes, and when physical activity fails to aid in the passage of gas and fecal material through areas of torsion or membrane constriction.

2. Walking or jarring, such as noticed during street-car riding or automobile riding will at times cause patients to hold their right sides to prevent the cramping sensation produced by constriction of the ascending colon by extraneous membrane—especially the perieto-colic and reno-colic group. A feeling of soreness in the right side also is relieved by pressure against the right side of the abdomen during exercise.

3. Patients with intermittent obstruction from pericolic membranes will observe periods of swelling in the region of the cecum and ascending colon which swelling fluctuates in size and is either gaseous or doughy to the palpating sense. This bulging mass frequently can be reduced by gentle massage upwards along the line of the ascending colon, with relief of the sense of fullness noticeable at the time the swelling is observed.

4. Cecal tympany often is present—the ballooned cecum, with impounded gas due to the constriction of the pericolic membrane across the ascending colon and hepatic flexure. Patients state that when tympany is present they are able to feel gas passing into the transverse colon during colicky attacks especially when passage is aided by massaging the colon upwards towards the hepatic flexure.

5. Solid and semi-solid fecal matter frequently can be palpated in the cecum and lower portion of the ascending colon, especially after periods of disturbance of the right colon attachments after exercise. Solid fecal matter, in the nature of an impaction, is not normal to the right half of the colon.

6. There is usually an absence of gas in the upper, ascending colon and hepatic flexure at a time when the cecum

is tympanitic, due to the constriction present at the upper portion of the ascending colon.

SYSTEMIC SYMPTOMS AND SIGNS

The systemic symptoms and signs are those common to patients suffering from intestinal toxemia arising from ascending colon constipation. The formation of a solid fecal mass in the right half of the colon adds to the difficulty of passage in the presence of constricting pericolic membranes attached to the ascending colon and hepatic flexure.

1. Patients often associate fatigue, a sense of lassitude and a tired feeling with their periods of distress in the right iliac region. Work is done with effort. This exhaustion frequently is noticed after physical exertion, or after an automobile ride which normally should produce an exhiliarating effect in those individuals not complaining of right iliac and right-sided pain as a result of the activity. It is very suggestive that these "nervous exhaustion symptoms" are a result of peritoneal shock possibly induced by repeated, subminimal, autonomic sensory stimuli reaching the central nervous system during exercise or activity.

2. There is present, in patients giving the other signs and symptoms of congenital pericolic membranes, a distinct tendency to nervous irritability after exercise which has induced pain along the right costal border posteriorly and along the right half of the colon laterally. Relatives frequently notice the increase in irritability of either children or adults after exercise; physical exertion may induce inflammatory changes in the pericolic membranes.

3. There is a noticeable tendency to underweight and undernutrition in this group of patients, especially in the period of adolescence and prior to full maturity. They complain of a difficulty in gaining weight; weight gained by forced feeding and bed rest notoriously is rapid in disappearing after the patient resumes the usual occupational interests. Weight loss frequently is more marked during periods of activity and partially regained by discontinuing physical activity and increasing the periods of rest. Much of the weight loss is in subcutaneous fat.

4. During attacks of discomfort occasioned by the pericolic membranes there is an associated muscular aching and muscular weakness.

5. Disturbances in circulation not infrequently are more noticeable during periods of mildly obstructive attacks. The degree of disturbances varies with the chronicity of the condition and the degree of stasis produced in the cecum. Cold, clammy hands and feet are present, and the patient uses artificial, external heat to the extremities when retiring. Vertigo is also a frequent complaint; this tends to disappear when meats are eliminated from the diet and an acidophilus culture regime is instituted. That the causative factor has not been eliminated by this procedure can be demonstrated by a recurrence of vertigo if the patient returns to a high meat diet and engages in those activities which produce pain and tenderness along the lateral aspect of the colon, with an increase in the sense of pressure and weight in the right half of the colon. Young adults with a definite pericolic-membrane-syndrome have presented vertigo as a major complaint. Minor seizures, simulating *petit mal*, have been observed only during periods when the right side was giving disturbance.

6. Headaches and backaches, although not pathognomonic, frequently are additional complaints. The backache, however, usually is localized over the region of the right kidney.

7. The skin of adults, who have been complaining of right-sided colic for a period of years, is often of a muddy, sallow color. This is usually true of any patient whose colonic elimination is slow and inadequate. Children with pericolic membranes, which are interfering with active elimination, may present icteric tinges to their skins whenever there is present an increased constriction in the pericolic membranes due to an increase in physical activity.

8. Constipation is present in over 50 per cent of the patients with the pericolic membrane syndrome, and when present, *dates from early childhood*, or "as long as I can remember." The so-called "reflex gastric symptoms" of constipation frequently are initiated by the constricting influence of pericolic membranes in the right half of the colon. The constipation in this group of patients usually does not lend itself to complete relief unless the patient abstains from physical exertion and the factors which produce disturbance to the pericolic membrane attachments to the colon. Diet and bowel habit are only of partial aid in the true mechanical interference with the normal passage of fecal content through the right half of the colon.

9. The scaphoid abdomen, with prominent anterior superior spines is by far the most frequent abdominal topography found in patients suffering from recurring attacks of right-sided colic due to pericolic membrane obstruction.

10. This group of patients often is found to have been undiagnosed on previous visits to their physicians and may be found among the group of so-called "chronic complainers," especially when the complaint is referred to the right lateral quadrant of the abdomen. The increased irritability and nervous exhaustion present at the time of the soreness and pain in the right flank, frequently label the individual as a "neurasthenic" complaining of his or her right side. It is probably more to the point that we have a patient complaining of right upper and lower quadrant pain, the long duration of which, coupled with the fact that he has "consulted doctors all over the country who have not been able to find the cause of my trouble," has been the real cause of the neurasthenia. Unrecognized, organized bases for gastro-intestinal disturbance probably are oftener responsible for a disappointed patient who after repeated attempts to obtain relief by medical means, finally loses hope and becomes introspective and a typical psychaesthenic. In some of these individuals, the typical exercise and right flank pain relationship can be found to date from early childhood, recurring periodically after exertion, exercise, etc., even though the appendix and the gall bladder have been removed in the hope of correcting this right flank pain and its associated undernourishment, easy fatigue and nervousness.

11. Enlarged mesenteric glands in the ileo-colic triangle is an almost constant finding in operations performed for partial obstruction of the ascending colon and hepatic flexure by pericolic membranes. These glands are present in varying degrees, at times independent of the type of chronic pathology encountered in the appendix. In one patient, a boy of 10 who had had an appendicectomy for "chronic appendicitis" at the age of 3 years, with no relief of right-sided colics associated with nausea and vomiting and undernutrition; mesenteric glands the size of lima beans were encountered only in the ileo-colic triangle and in no other portion of the mesentery of the colon or small bowel. These glands lay proximal to the point of narrowing of the ascending colon and were associated with a dilated cecum exhibiting no acute inflammation. This may be the explanation of many cases of so-called *tabes mesenterica*, and some of the reported cases of ileocecal glands. There is no doubt but that there is an increase in the absorption of toxins from a dilated cecum, when the mucous membrane is stretched by distention of the cecal wall and with the glands representing the first line of lymphatic defense.

SYMPTOMS AND SIGNS OF A REFLEX NATURE ARISING IN THE GASTRO-INTESTINAL TRACT—PROXIMAL AND DISTAL TO THE POINT OF CONSTRICTION—BY CONGENITAL PERICOLIC MEMBRANES

1. Gastric disturbances rarely are absent during periods of attacks of colics or pain in the region of the cecum, ascending colon or hepatic flexure, especially if induced by occupational activity or physical exertion.

2. The appetite, as a rule, is poor or indifferent during periods of soreness along the lateral border of the right portion of the colon. This is particularly true in children and young adults with a definite pericolic membrane syndrome, in whom the appetite becomes capricious after strenuous exercise or whenever there is a period of soreness along the lateral attachment of the colon, especially in the right lumbar area.

3. Attacks of nausea and occasionally vomiting may be present after strenuous exertion, play, or occupations requiring lifting, and after long automobile rides in patients complaining simultaneously of pain along the lateral borders of the ascending colon and cecum or hepatic flexure. The right lower quadrant soreness, associated with nausea and vomiting presents a clinical picture suggestive of appendicitis. Absence of temperature and the presence of a normal leucocyte count, however, in most instances do not admit a diagnosis of acute appendicitis. Rest, enemata and cold compresses usually help to allay the "attack." Frequent recurrences of this type often induce the surgeon to perform appendicectomy alone, which, however, seldom relieves the mildly obstructive symptoms induced by the rotation of the ascending colon near the hepatic flexure; persistence of preoperative symptoms with the tender cecum is frequently seen.

4. A sense of fullness, while eating and immediately after meals, with belching after meals and a sense of pain in the pyloric area (pylorospasm) are some of the more common reflex epigastric symptoms observed during disturbances arising from pericolic membrane obstruction of the right colon. These symptoms have been given equal importance in cases of so-called "chronic appendicitis," but still may be present after appendicectomy and only relieved when the true nature of their etiology has been discovered. A truly "reflex type of dyspepsia" is present in the uncomplicated case, with relief when the stomach is empty, and distress which begins when food enters the stomach.

5. Recurring "bilious attacks" associated with colicky pains and soreness along the right costal border in the region lateral to the liver must be considered as of a mildly obstructive nature, especially if some of the other factors enumerated above are present. Neoplastic lesions of the right half of the colon, must be considered along with hepatic, cholecystic and appendiceal pathology before the diagnosis of the presence of mechanical obstructions of the ascending colon and hepatic flexure can be seriously entertained.

6. Spasticity of the sigmoid has been found to be an almost constant factor in well-substantiated cases of mechanical interference with the function of the cecum, ascending colon or hepatic flexure. This becomes more marked during periods of active disturbance, with a palpable sigmoid, tender to touch and with the patient experiencing a sense of flatulence for the period of the discomfort on the right side. This condition frequently is treated as a "spastic colitis" and considered primary, whereas, a careful history-analysis will unfold the true primary etiological factor. Inflammatory lesions of the appendix and the gall bladder will give a similar spasm of the sigmoid and the descending colon.

IMPROVEMENTS OBSERVED AFTER SECTION OF CONSTRICTING PERICOLIC MEMBRANES AND APPENDICECTOMY

It would be reasonable to assume that if the above syndrome were established as an entity, that a correction of the mechanical disturbance with the function of the right half of the colon should result in a subsidence of those symptoms presumably attributed to their interfering presence. That this occurs has been demonstrated clinically both in the group of patients who have failed to obtain relief of their symptoms by appendicectomy or cholecystectomy, or both, when the symptoms, signs and roentgen studies pointed towards an intermittent obstruction of the right half of the colon; and by those in whom an appendicectomy was done when the findings in the appendix did not seem to explain the patient's symptomatology but in whom definite obstructive phenomena were noted in either the lower ileum or the ascending colon and hepatic flexure.

Some of the improvements noted by patients are referred specifically to the factors mentioned in the syndrome above cited. There is a relief of the sense of "drag" in the right flank and right lumbar region; and the former feeling of pain, fullness, and distension of the right side of the abdomen gradually disappears. There has been a satisfactory improvement in the ease of elimination, bowel habit is more easily established and colonic lubricants are used in diminishing amounts, whereas constant attention to elimination was the rule before.

The former tendency to attacks of fullness after meals, eructations and nausea, gradually disappear as begin improvements in colonic elimination, naturally produced.

Appetite returns to the point where food is relished and the tendency to anorexia after exercise, is lost. The degree to which the return of appetite is noted is somewhat dependent upon the duration and severity of the patient's obstructive phenomena occasioned by pericolic membranes. Foods, which previously disagreed, are taken with comfort and enjoyed. There is a consequent gain in weight, from five to twenty pounds in the first six months and physical strength and endurance are increased. There is less fatigue and the exaggerated nervous irritability which the patient frequently exhibited, is markedly diminished or lost entirely.

The facial expressions, in exaggerated cases, have lost their drawn, haggard appearances and the skin color tends to become clear, often losing the yellowish brown tinge.

It has been noted that, as a rule, the longer the duration of symptoms pre-operatively, (especially when associated with an atonic, dilated cecum) the slower is the convalescence. The return of tone to the right half of the colon can be noted by a gradual improvement in elimination and by a diminishing number of reflex gastric symptoms.

ROENTGEN EVIDENCE OF FUNCTIONAL OBSTRUCTION BY CONGENITAL PERICOLIC MEMBRANES

The author was surprised, during the early part of this study, by the frequency with which these membranous constrictions were missed by the roentgenologist. This, in spite of the fact that some of our patients were unable to perform active work and were having definite symptoms at the time of the examination. Negative findings were reported in the gastric, duodenal and colonic roentgen studies in patients who demonstrated definite constrictions at the time of operation with lateral torsion of the colon in the region of the hepatic flexure and marked dilatation of the cecum. The complete relief of symptoms and the clinical improvement which followed section of the constricting membranes and a freeing of the hepatic flexure led the author to suspect that possibly the technique employed in the giving of the usual barium enema was at fault and that the roentgen examination produced an artifact by the distention of a flexible bowel wall with a non-compressible heavy semi-fluid medium. This mass easily distended the bowel beyond normal physiological limits and opened the lumen by pressure *from within*, whereas the patient's difficulties were caused by membranes which produced disturbance *from without* by resisting the passage, intermittently, of normal physiological substances as semi-soft fecal masses and intestinal gas. It was found that, on several occasions, the diagnosis of congenital pericolic membranes was confirmed in a cholecystic study, which gave normal gall bladder findings, by a cecum filled with gas which narrowed to a small lumen in the proximal portion of the hepatic flexure, *i.e.*, a "pear-shaped" appearance of the right colon with no gas in the part of the transverse colon visible on the plate. This was later verified by the technique to be described.

In order to eliminate the possibility of producing abnormal roentgen findings by unnatural means of study the following technique was devised.

SPECIAL ROENTGEN TECHNIQUE

1—Patients are given a pint of barium by mouth 24 hours before the colon study is to be done.

2—Before giving the barium enema, the location of the barium column from the above meal is fluoroscopically noted and a plate is made.

3—The usual barium enema technique is now employed, using very little elevation of the barium container by the gravity method. During the slow passage of the barium into the bowel, the points are noted at which the barium column is found to hesitate, and appearances of areas of spasm noted. Any hesitation of the barium column, requiring a dilatation of the colon before the barium head passes on, is noted, especially when this occurs in areas in which spasm is more or less infrequently found. The entire colon is then filled without undue pressure and a plate taken.

4—The patient is then permitted to expel the barium enema and an air injection made slowly with a small hand-bulb attached to a rectal catheter. The column of air is followed by fluoroscopic observation to prevent an abnormal distension of gas and to observe points along the length of the colon where the air seems to require dilatation of the colon before its passage is permitted. A plate is then taken.

5—It is of interest to note that the air injection carefully done, will give the most diagnostic plate of the series together with the 24 hour film. So-called "gun-barrelling" of the ascending and the transverse colons can be identified by this means whereas the overlapping of the barium column in the opaque enema fails to give this finding. During fluoroscopy, with a heavy mass in the colon, the two portions of the hepatic flexure seem to separate under the palpating hand, whereas, in the air injection the narrowing and close contact of the two narrowed portions seem to prevent the intracolonic air from distending this portion to the same degree that is present elsewhere in the colon.

Patients have also noted a recurrence of the typical right upper flank pain, common to their attacks, when barium or air is passing through this constricted area.

The above technique may not be the best method one might employ in the detection or verification of this group of cases by the roentgen ray but is a method the author has found useful *in lieu* of the usual barium enema introduced with considerable gravity pressure.

DIAGNOSIS OF THE SYNDROME OF CONGENITAL PERICOLIC MEMBRANES

The diagnosis of symptomatic, congenital pericolic membranes frequently will be suggested from a carefully taken history-analysis which considers the above-outlined syndrome.

When carefully elicited, the symptoms of "exercise-pain in right side" relationship can be frequently elicited as dating back to early childhood. The relationship between pain in the side and reflex gastro-intestinal phenomena of childhood is frequently missed, particularly if the preceding physical activity factor is not elicited in the history. Appendicitis is considered, but excluded when laboratory findings fail to substantiate the clinical picture. Constipation, intestinal colics, nausea and vomiting, failure to gain weight, capricious appetite and variable periods of nervous irritability are frequently associated phenomena suggesting a diagnosis of congenital pericolic membranes. These symptoms are especially significant when present after an increase in activity. Duodeno-jejunal angulations (ligament of Treitz)—with obstruction, ileo-pelvic bands (Lane), ascending colon constrictions, and hepatic flexure constrictions produce a definitely aggravated symptomatology after exercise or hard play, especially in children and young adults. The "side-aches" usually correspond in location with the right upper flank, under the right costal border, and in the pelvis, when due to ileo-pelvic bands. These children and young adults frequently will consult their physician for permission to be excused from organized gymnasium curricula of the public schools because of the right-sided and reflex gastro-intestinal symptomatology produced as a result of activity.

Symptoms of congenital pericolic membranes may develop after an attack of whooping cough or severe, prolonged cough of a respiratory tract infection. The persistent tugging against the right reno-colic ligament produces an inflammatory reaction in this membrane, with an increase in the amount of fibrous tissue, causing an accentuation of these attachments. For months after the attack of cough subsides, the accentuated fibrous connective tissue membrane contracts and shortens and causes a marked increase in the symptoms. Several such cases have been observed by the author where the onset of right flank symptoms has dated from such an onset.

TREATMENT

Since the scope of this paper deals with the diagnostic syndrome of congenital pericolic membranes the question of treatment will be presented in a later paper when the author's case reports and follow-up data will be presented together with methods employed in the correction of these mechanical interferences with physiological function of the small and large intestine. Mechanical causes for intestinal malfunction, however, frequently require mechanical correction after a carefully controlled, non-effective therapeutic management.

CONCLUSIONS

1. The symptom-complex of many cases of so-called "chronic appendicitis" has long been suspected of being a mixed syndrome, whose symptomatology is not always relieved by simple appendicectomy.

2. The signs and symptoms of a syndrome produced by congenital pericolic membranes, is presented with the hope that it may aid in clarifying some of the obscure symptoms often found associated with chronic right abdominal symptomatology.

3. The "congenital-pericolic-membrane-syndrome" may explain some of the cases of unrelieved right-sided upper and lower abdominal chronic symptomatology attributed to low grade infections in the gall bladder and appendix but not relieved by the removal of the gall bladder or appendix, or both.

4. The relationship between physical exercise and activity and the subsequent symptomatology produced presents an important factor in the diagnostic syndrome of congenital pericolic membranes producing local and systemic symptoms.

5. Roentgen-ray findings frequently are misleading when the technique commonly used to detect organic infiltrative or neoplastic lesions of the colon has been employed. A method is suggested which uses a compressible contrast-medium, air, rather than the heavy, liquid non-compressible medium so diagnostically effective in other types of colon pathology.

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ACUTE LIVER DEGENERATION: TREATMENT BY CHOLECYSTOGASTROSTOMY*

WITH DISCUSSION OF THE CLINICAL, PATHOLOGICAL AND PHYSIOLOGICAL ACCOMPANIMENTS

By

CHAS. GORDON HEYD, B.A., M.D., F.A.C.S.

NEW YORK, N. Y.

THE designation "catarrhal jaundice" long has been a misnomer. The naming of a condition after its most prominent symptom or sign no longer is tenable nor is it possible to suppose that extrahepatic infection of the bile ducts or of the papilla of Vater is the main factor in the production of this type of jaundice. According to Klemperer, Killian and Heyd,[1] so-called *icterus catarrhalis* neither is a morbid or a pathological entity. However, three forms may be differentiated: (1) an icterus due to obstruction of the common duct, incident to or following a gastro-intestinal "catarrh;" (2) an icterus due to degeneration and multiple necroses of the liver, which pathology is hematogenous in origin and which is associated with pneumonia, rheumatism, typhoid and other septicemic states; the etiological factor of this group is not known but various types of bacterial toxins have been indicted as causative; (3) an icterus due to cholangitis and which results in a blocking of the intrahepatic bile radicles; the cause of this condition probably is of hematogenous origin.

The diverse clinical and pathological elements in acute liver degeneration may be expressed by a consideration of the following patients:

CASE 1.—*B. K.,*[2] *Chart No. 34,* female, married, aged 10, entered the New York Post-Graduate Hospital, February 25, 1925, complaining of *pain* in the right upper quadrant, and a progressively increasing jaundice of one month's duration.

About one month previous to admission to the hospital, while on the street, she had a chill and upon returning to her home noticed a rash on her right forearm. This *eruption* spread over her entire body but disappeared in two days, at which time she began to have pain in the arms, legs, and fingers, accompanied by swelling. "The hand was so swollen that she could not make a fist of the fingers." At the end of a week the swelling had disappeared and the pain had changed to "a sensation like needles over all of her body."

About a week later, the patient began to have *pain in the epigastrium* on the right side under the ribs. This pain became so severe as to be almost intolerable. At the time the patient complained of severe colicky pain, her *stools became "white,"* and *jaundice* appeared. During this period she vomited only twice, both times after eating meat.

Physical examination: The patient was a well-nourished, middle-aged woman, intensely jaundiced. The right pupil was somewhat smaller than the left but both reacted to light and to accommodation. On *abdominal examination* the liver was easily palpated, six cm. below the costal margin in the nipple line; tenderness was marked and there was considerable spasm on inspiration. The remainder of the physical examination was not noteworthy. The *clinical diagnosis* was "catarrhal jaundice," although a leutic hepatitis was considered.

During the patient's stay in the hospital the jaundice became progressively more intense and she began to develop stupor tending towards coma. *Laboratory studies:* The Wassermann was negative. The coagulation time was seven minutes. The bleeding time was ten minutes, and at blood grouping, she fell into group two. Examination of the urine revealed a moderate amount of albumin, 0.30 per cent. sugar, but was negative for diacetic acid and acetone. Microscopically, there were a few white cells and amorphous urates. Previous to operation the blood serum analyses were as follows:

Date	N—P—N	Urea N	Amino Acid N	Cholesterol	Fibrin	Icterus index	Van den Bergh		Dye Test	
			Mg. per 100 c.c.				direct	indirect	15 min.	60 min.
2/27/25	31.9	8.3	7.2	160	340	225	++++	++++	15	20
3/2/25						220	++++	++++		

TABLE 1. *Blood Serum Studies—Case 1. Before Operation.*

In view of the patient's increasing jaundice and the development of stupor, the clinical diagnosis was changed and a provisional diagnosis was made of *chronic cholemia due to possible malignancy, and extrinsic occlusion of the common duct.* An intravenous injection of 10 c.c. of four per cent calcium chloride was given.

Operation: On March 4th an exploratory laparotomy was performed. The liver was about one-third larger than normal, with apparently normal edges, although there was some slight evidence of an interstitial hepatitis. The liver generally suggested a biliary stasis and was otherwise not noteworthy. The gall bladder was about twice its apparently normal size, but not markedly distended. The pancreas appeared normal on palpation. No calculi were determined in the gall bladder or the common duct nor was any apparent mass within the pancreas. The stomach and duodenum were negative.

The absence of any demonstrable gross pathology sufficient to account for her jaundice, except possibly the rather distended gall bladder, caused much doubt as to whether any further operative procedure should be carried out. It was not apparent that biliary drainage would help her and it was evident that the loss of bile through an external fistula was not a desirable thing; no bile was being delivered into the intestine.

In the desire to allow the bile to enter the gastro-intestinal tract and because of the possibility of small overlooked calculi in the *ampulla* of Vater, a *cholecystogastrostomy was performed;* at the same time a small section of the right lobe of the liver was removed for histological examination. It is interesting to note that, following the cholecystogastrostomy, for forty-eight hours the jaundice became more intense. On March 6, a note by Dr. Donaldson stated that the jaundice had deepened but that the patient felt much better. Blood analyses following the operation are particularly interesting as showing the gradual clearing up of the jaundice and its accompaniments.

Date	N—P—N	Urea N	Amino Acid N	Cholesterol	Fibrin	Icterus index	Van den Bergh		Dye Test	
			Mg. per 100 c.c.				direct	indirect	15 min.	60 min.
3/10/25	33.0	13.7	6.5			80	++	++	7.5	10
3/18/25	22.4	7.5	7.0	166	340	52	++	++	0	4
3/26/25						15	—	+		
4/29/25	30.0	12.5				10	—	+	5	0

TABLE 2. *Blood Serum Studies—Case 1. After cholecystogastrostomy.*

The small *portion of the gall bladder* removed in making the cholecystogastrostomy *ostium* on *histological examination* showed no evidence of any pathological change. The pathological report upon the liver tissue showed that the lobular structure was easily recognizable. The Glisson's capsule was thin and several lobules near this surface, as well as in the deeper areas, showed changes within the center of the lobules. The changes were characterized by the disappearance of liver cells to such an extent that the center of the lobules showed only a framework without liver cells. In these areas of the liver lobules there was a proliferation of the endothelial cells and numerous lymphocytes and occasional polymorphonuclear leucocytes were to be seen. The liver cells, particularly near the centers, which were preserved, showed parenchymatous degeneration occasionally with karyolysis. There was only a small amount of bile pigment recognizable in the cells. The picture was that of a central necrosis of the liver lobules. It could be compared with the changes of acute yellow atrophy, only it was of a much milder degree. (Figures 1 and 2). The gall bladder showed regular rugae. The gall bladder wall was devoid of pathological changes.

Discussion: This case aroused the interest of both the laboratory and clinical sides of the service. Repeated study and consideration finally convinced all that the patient's first manifestation of trouble was an acute febrile condition, simulating in character, acute articular rheumatism; from this there was sustained an intense and progressive injury to the hepatic parenchyma, resulting in the histologic picture of severe, central necrosis of the liver lobules. While the slides do not show the outstanding features of acute yellow atrophy, they do suggest the same type of lesion, only of much milder degree. After the intoxication had passed its critical point,

*From the Surgical Clinic, New York Post Graduate Hospital.
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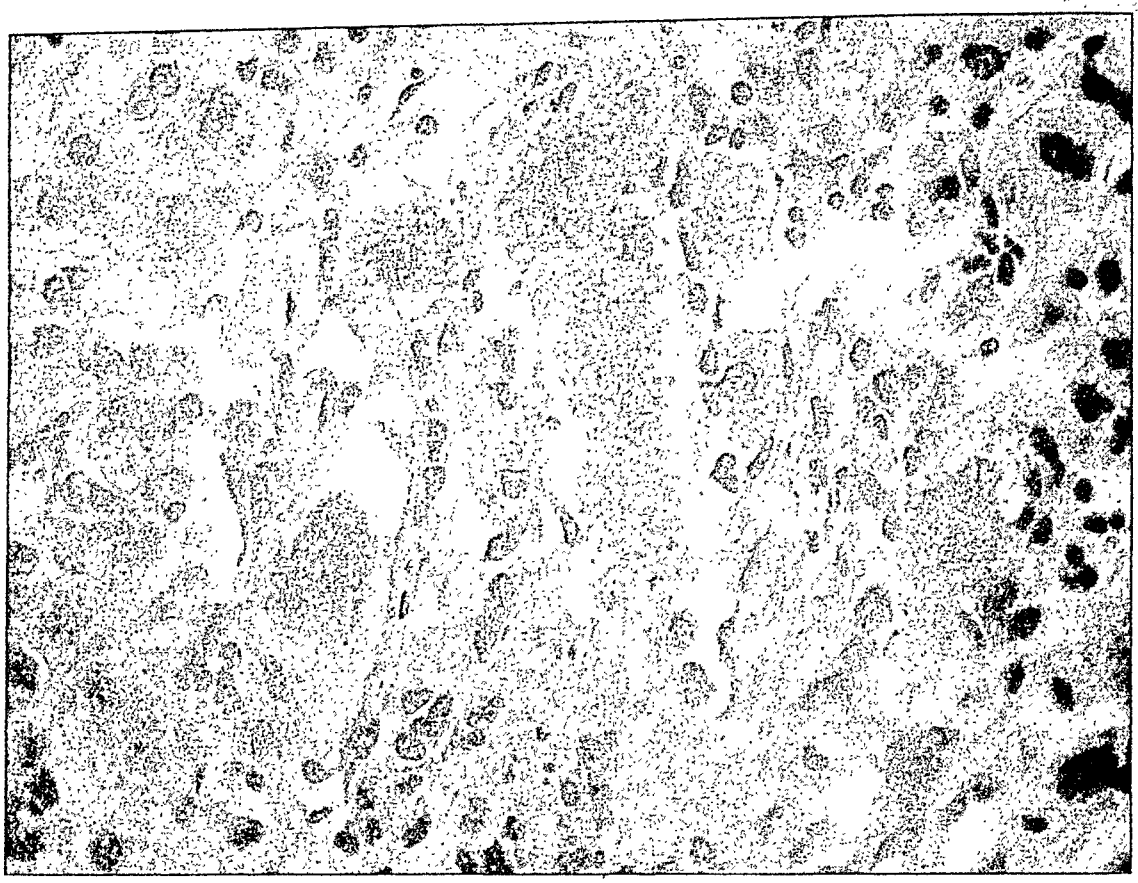


Figure 1—Photomicrogram showing liver cells with granular degeneration and various stages of karyolysis, ending with complete nuclear disappearance.

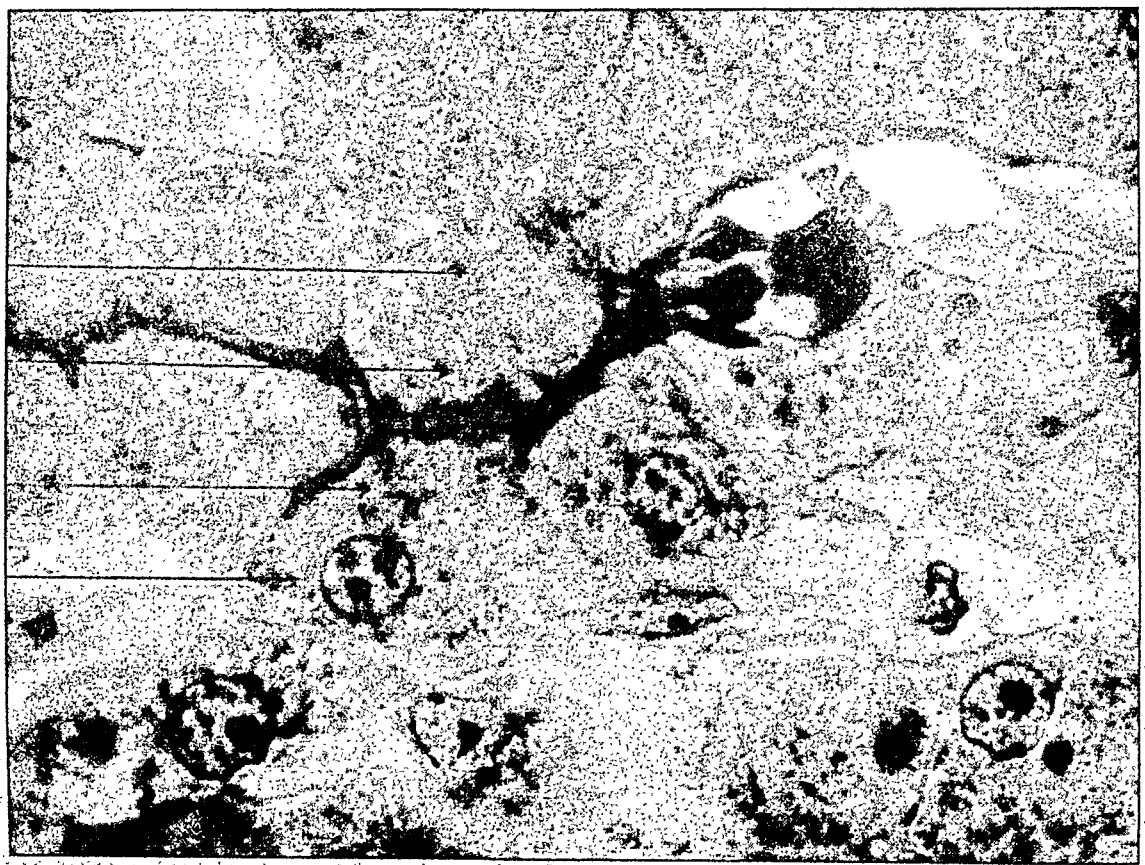


Figure 2—Photomicrogram exhibiting rupture of intracellular bile capillary with extravasation of bile.

there occurred a normal regeneration of liver tissue. The patient has remained permanently well. It is interesting to note that she has had no discomfort from the presence of a cholecystogastrostomy.

In July 1926 this patient, after an uneventful pregnancy, was delivered of a living normal child and has enjoyed excellent health to date. The pregnancy indicates a remarkable recovery from a grave liver injury and exhibits the unusual degree of regenerative power possessed by a liver after an acute, toxic or septic systemic, degenerative status.

CASE 2.—*D. R., Chart No. 18106*, male, aged 20, entered the New York Post-Graduate Hospital, October 6, 1926, complaining of jaundice, nausea and vomiting; weakness, mental depression, and with a loss of twenty pounds during the preceding six weeks.

The patient's illness began about two months previously with fever and weakness. He stated that he ran fever for three days and, at about the same time, began to lose strength and weight and was frequently nauseated. About two weeks after the onset of fever the patient became *jaundiced*, this increased in intensity for three weeks and began to fade away. After an interval of a few days during which the jaundice was distinctly diminished, again there occurred an increase in the intensity of the icterus accompanied by fever and vomiting, these symptoms becoming more frequent. There was no pain, although there was considerable belching and eructation of gas. Patient stated that his *stools were gray in color* but otherwise not abnormal. He had had a mastoid operation, a septum operation, and adenoids and tonsils removed some eleven years previously.

When the patient was admitted to the hospital he was intensely jaundiced; there was marked *itching* but *no petechiae. Physical examination* was negative except for tenderness in the right upper abdominal quadrant; both liver and spleen were palpable. The *tentative diagnosis* was "obstructive jaundice," possibly of toxic origin.

Laboratory studies: The leucocyte count was 11,800, with 74% polynuclears, polynuclearphils, red cells 4,952,000 per cubic mm., haemoglobin 96%, platelets 224,600 per cubic mm., Wassermann was negative, the *icteric index was 100; Van den Bergh direct* +, *Van den Bergh indirect* +++, *Fouchet* +++. Later, on October 17th, the *icteric index* was 166.6, *Van den Bergh direct* ++++, *Van den Bergh indirect* ++++, *Fouchet* ++++.

X-ray examination of the gall bladder region revealed no evidence of calculi. The right lobe of the liver was markedly enlarged, but its free border quite smooth. X-ray examination of the kidneys was negative. X-ray examination of the gastro-intestinal tract was negative except that, at the end of twenty-four hours, there was considerable irregular distribution of the barium meal suggesting colonic spasm; stasis also was observed in an irregularly filled, segmented appendix.

The *stools* were uniformly *clay-colored* with the chemical test for bile slightly positive.

The patient's course was continuously downward; jaundice increased in intensity; mental depression and pruritis were pronounced. Vomiting became a prominent feature for ten days prior to operation.

At operation, October 20, 1926, the liver was found to be about twice the size normal for the patient's age, weight and stature. There was no evidence of fibrosis of the capsule of Glisson. There was about 300 c.c. of pale-amber, ascitic fluid in the abdomen. The gall bladder was thickened but without stones; increased thickness of the gall bladder wall was apparently due to edema. The common duct was narrow, not thickened nor dilated. The lymph-glands at the junction of the cystic and common ducts, were enlarged. The pancreas, if anything, was softer than usual. The gastro-doudenal segment was negative. The lower abdomen was not explored: the appendix was left *in situ*.

Operation consisted of a cholecystogastrostomy with the application of the gall bladder to the lesser curvature of the stomach about three cm. from the pyloric ring. The suture line was reinforced by wrapping a portion of the greater omentum about it and a small cigarette drain was inserted into "Morrison's space."

Aside from nausea which lasted for six days the post-operative convalescence was uneventful. Seven days after operation the icteric index dropped to 101, while the Van den Bergh direct and indirect were still ++++ and Fouchet ++++. Two weeks after operation the icteric index was 65, Van den Bergh direct and indirect +++, and Fouchet +++. From this time on, the patient had a constantly diminishing jaundice and was discharged on the twenty-sixth day after operation with normal colored stools and practically free from jaundice, although the sclera were suggestively yellow.

Discussion of Case 2: The patient presented a condition characterized by intense progressive jaundice that was sequential or associated with a febrile attack. The clinical and chemical evidence was such as to suggest complete biliary duct obstruction. The opinion of the attending physician was that this patient had had an initial attack of influenza. The stools in the beginning were bile colored but, later, became "clay colored" due to practically an entire absence of bile. The gall bladder was not palpable nor had there been any suggestion as to the applicability of Courvoisier's law. X-ray studies did not reveal any gross gall bladder disease. The liver, at laparotomy, was smooth and glistening and of normal color but about twice the normal size. There was no evidence of interstitial fibrosis such as is observed in the liver in long-continued abdominal affections and gall bladder disease. The gall bladder, itself, was edematous and hypervascularized; it did not contain bile but only a colorless mucoid material. The cystic and common ducts were not obstructed although edematous.

It would seem that the underlying pathology in this patient was an infectious or toxic condition with degeneration of the hepatic parenchyma. As a result of the destruction of the liver cells, probably the bile *canaliculi* became blocked with broken down cellular detritus and bile thrombi. Apparently, the cytoloysis of liver cells continued resulting in collections of bile into so-called "lakes." Seemingly, there were two pathological factors at play, (1) the primary destructive action as the result of a blood-borne agent and (2) the mechanical obstruction of small bile *canaliculi*. The final result, so far as the liver was concerned, was the development of a marked edema of the entire liver, a condition well described as "hydrohepatosis." These changes can be followed in the histological examination of the specimens of liver removed at the time of operation.

The question arose as to what benefit could be expected from a cholecystogastrostomy. The surgical indication in this patient was to deplete the liver-tissue of its fluid; in other words, to relieve the passive congestion and edema. This could have been accomplished by multiple incisions in the liver, but resultant hemorrhage contraindicated such procedure. The only other way of producing a loss of fluids and of relieving the edema present was the devising of an adventitious pathway for lymphatic drainage. This could be accomplished either by a cholecystostomy or a cholecystogastrostomy. In the former there would have been the loss of bile, a factor not to be lightly considered, and in the latter procedure there would be established a lymphatic depletion of the liver with delivery of bile into the gastro-intestinal tract. This was the reasoning which prompted us to do a cholecystogastrostomy in the presence of an obstructive jaundice which apparently was within the liver and in the presence of normal gall bladder and external biliary passages.

The preliminary diagnosis was "chronic jaundice secondary to acute influenza." In spite of the most approved medical therapy, including the Lyons' method, the patient progressively became worse and in the opinion of three consultants was considered hopeless. From their previous experiences, it was suggested that a cholecystogastrostomy be done irrespective of the pathological condition which was causing the obstruction. This was carried out and the patient progressed to complete recovery.

In searching for an explanation for the cure of this patient, one can only assume that the cholecystogastrostomy provided a means for relieving the edema and congestion of the liver. Previous histological studies of the liver showed the remarkable destruction of liver tissue and an associated extensive edema. It is well to recall that the greatest degree of liver enlargement in acute hepatic necrosis is due to the serum that is present in the gland. Experimentally, it has been demonstrated that upon removal *in toto* of an acutely degenerated liver and suspending it, as much as 500 to 1000 c.c. of water can be obtained by gravity drainage. Before operation, the gall bladder did not contain any bile and no bile was present in the gastro-intestinal tract, yet forty-eight to seventy-two hours following cholecystogastrostomy, bile was present in the stomach. Within ten days the icteric index dropped to 67. This case may be one of opportunism in that the patient seemed on the way to recovery irrespective of what was done but it is reasonable to suppose that surgery changed some of the hydrostatic mechanism in that liver and allowed hepatic regeneration to take place.

GENERAL DISCUSSION

In an "hepatic unit" (*hepatons* of Rossle) there is a capillary arising from the portal system and this is separated from the hepatic cells by a lymphatic space. If there is degeneration of the liver cells, this lymphatic space is increased in size by becoming filled with protein derivatives; an inflammatory or toxic edema results. Probably, it was this mechanism which was present in the cases cited.

Under ordinary circumstances the liver has remarkable detoxifying and lytic properties; it is able to dispose effectively of hematogenous poisons and bacteria themselves. Apparently, under conditions of normal health, bacteria appear from time to time in the bile: the injection of colon or typhoid bacilli into the veins of the ears of rabbits is followed by their appearance in the bile. There, they may persist for many weeks either in the bile or in the gall bladder.[4] Adami[5] demonstrated that the gastro-intestinal tract is capable of allowing the passage of bacteria through its wall. In a series of *post-mortems*, which Adami and Nichols studied in detail, they found that the glands in the right side of the abdomen, (particularly that chain of glands that goes from the appendix up along the ileocolic artery and which passes beneath the greater curvature of the stomach to connect with the lumbar lymph glands), were infected with viable bacteria. Furthermore, they demonstrated polymorphonuclear leucocytes loaded with bacteria in the act of passing through the intestinal wall. In certain conditions, bacteria constantly were found in the bile together with the byproducts of bacterial destruction in the blood from the spleen. Many years ago Vidal[6] in his work on cirrhosis of the liver effectively demonstrated that the detouring of the portal blood by an "Eck's fistula" invariably resulted in death from general septicemia in from four to six weeks.

Theoretically, the liver can be injured by (1) bacteria or toxins reaching it through the general blood stream, (2) bacteria or toxins reaching it through the portal blood and (3) toxins or bacteria reaching it through the bile-duct system. The demonstration by Sudler[7] of the intimate lymphatic connection between the gall bladder and liver and the subsequent emphasis placed upon it by Graham[8] indicates the possibilities of liver damage under the ordinary conditions of living. It has been repeatedly demonstrated that cirrhosis of the liver is not produced experimentally by the ordinary toxins of the intestinal tract but that if the element of *infection is added to toxic conditions*, cirrhosis follows with marked frequency[9].

The liver stands alone in its unique property of regeneration. If the injury to the liver is not too severe or too precipitous, regeneration occurs *para passu* with degeneration; the final result may well represent a complete functional recovery as in Case 1, where the patient subsequent to illness and operation, had a normal pregnancy and nine years after operation is enjoying excellent helath.

Pathological—physiological considerations: After laparotomies there is absorption of normal or altered blood serum, pathological exudates and the byproducts of a deranged gastro-intestinal system. The absorption of any great amount of wound serum means an increased burden upon the liver. Wound serum is essentially protein material which must be metabolized by the liver after its absorption. In all laparotomies there are varying degrees of peritoneal denudation and particularly after certain pelvic operations. In all these cases there is peritoneal transudation and some wound secretion. Drainage is indicated in these cases not alone to prevent the development of sepsis but also to allow for external drainage of the accumulated wound secretions which might otherwise embarrass an already overburdened liver. Experimentally, it has been demonstrated that the injection into the circulation of the secretion from any large intraperitoneal wound is injurious to the hepatic parenchyma; the effect of such injections can be chemically estimated as a decreased output of bile acids and bile salts. The most beneficial technical detail is to aspirate as much fluid from the operative field as is possible and to plan the surgical procedures so as to leave a minimal amount of abraded or denuded peritoneal surfaces. In this regard, it appears wiser also after a cholecystectomy, for acute or subacute cholecystitis, not to suture the two edges of the gall bladder *fossa* together since the ability of the liver "to weep" hepatic serum for absorption by the peritoneal lymphatics rather than by the liver itself, means a lessening of the load imposed upon that organ[10].

Operative cautions: From a practical standpoint the following details should be watched carefully both before and after operation: the maintenance of a normal water balance; increase the glycogen reserve function of the liver; prevent acidosis and alkalosis, and hypochloremia. Water circulation in the liver-small intestinal segment is approximately 10000 *to 12000* c.c. a day, and the maintenance of this circulation is essential to the preservation of life. According to Orr[11] water loss of 10 percent is associated with serious complications, while a loss of 20 to 22 percent of water invariably is followed by death. Gall bladder and liver diseases which are associated with marked or persistent vomiting entail a rapid loss in chlorides; such is a step toward hypochloremia. The important indication is to restore the chloride balance by the intravenous administration of 100 to 200 c.c. of two percent solution of sodium chloride before such serious complication arises.

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SECTION VII—*Surgery of the Lower Colon and the Rectum*

DIVERTICULITIS OF THE COLON (WITH ABSCESS FORMATION) INITIATED BY TRAUMA FROM AN ENEMA TIP*

By
JEROME M. LYNCH, M.D., F.A.C.S.
and
MAX P. COWETT, M.D.
NEW YORK, N. Y.

IN the medical literature from time to time one reads of accidents, resulting from enemeta, but after making an exhaustive survey, the authors have failed to find an instance where an abscess (diverticulitis) has resulted from direct trauma by an enema tip.

The mere existence of diverticula does not necessarily involve ill health, any more than does the presence of a vermiform appendix. The work of Spriggs and Marxer, Lockhart-Mummery, Judd, Case, Mayo, Beer, Lynch, Rokitansky, Ball, *et al.*, has shown that diverticula occur in the large colon in about ten percent of individuals past forty, without the subjects experiencing any inconvenience.

The *pathology of diverticulitis* and appendicitis is similar. So long as the normal bowel contents are free to escape, there is no trouble, but if the fecal mass be abnormal or too long retained or if the virulence of the bacteria be enhanced, the organisms may invade the tissues. The result may be merely a catarrhal swelling of the mucosa with further obstruction, an abscess may form and burst inwards, leaving an ulcer, or burst outwards leading to peritonitis. Adhesive inflammation may lead to attachment of sigmoid to the urinary bladder, to numerous parts of the intestinal tract or to the uterus or its adnexa.

Diverticula rupture and cause abscess formation, when there is any increase of intra-abdominal or intra-colonic pressure. Cases have been reported in which diverticulitis has been caused by drastic catharsis.

The following case is reported because it demonstrates the danger of faulty instrumentation or the promiscuous use of enemata in the presence of pathology in the rectum, sigmoid or pelvic colon. From the sequence of events which occurred, in the opinion of the writer, the enemata (trauma) was the causative factor in producing the abscess.

CASE REPORT

J. B., aged 51, Negro, married. Occupation, veterinary assistant. Family history: essentially negative. Previous history: no illness or operation. Venereal disease denied by name and symptoms. Married 31 years. Five children alive and well. Wife had one miscarriage. Habits: always lived a moderate, temperate life. Has had no gastro-intestinal complaints. Ever since he can remember has had two regular bowel movements a day, one in A.M. and one at night. Never noticed any blood in stools. Denies ever having diarrhoea.

Present illness: Patient first came to Polyclinic Hospital Dispensary (G. U. Clinic) in October 1933, complaining of inability to hold urine—urgency, nocturnal polyuria, (4 to 5 times).

Physical examination: Prostate is moderately enlarged and boggy. There are strictures in the anterior urethra. Patient came to the G. U. clinic on two or three occasions but at no time was a satisfactory catheterization of his ureters made. Was told to prepare himself by a soap-suds enema and return to the clinic on the morning of February 23, 1934.

At about 6:30 A. M. on February 23rd, the patient gave himself a soap-suds enemata, allowing about one-fourth of the contents of a two quart bag to run into the rectum before he got a desire to evacuate; he passed some hard fecal masses and, according to his own statement felt better. He then inserted the enema tip further: as soon as he let the water run, he experienced a sharp, cramp-like pain in the left lower iliac region. The pain was so severe that he had to lie down. It became gradually more severe and his abdomen became distended. However, he was able to walk to the clinic (one block). An attempt was made at pyelography, but this maneuver intensified his symptoms. Before long the pain was so great that the patient exhibited signs and symptoms of shock. He was admitted to the hospital from the Cystoscopic Clinic because of this acute abdominal pain.

Diagnosis on admission: Chronic cystitis, obstruction of left ureter, ureteral colic.

Course in Hospital: Physical examination was essentially negative except for a distended abdomen and tenderness in both flanks, more marked on left side. Temperature 100.8, pulse 102, respiration 20, blood pressure 114/82, white cell count 9,200, polys. 68%. February 24th: *Medical consultation*—Fatty abdominal wall, slightly distended. No rigidity. Rebound tenderness over lower left region. Impression: trauma to the lower sigmoid by enema tip. Advise proctological consultation. February 26th: General condition of patient was better, although he is still tender over descending colon. Has been passing a considerable amount of mucus, tinged with blood.

Proctoscopy attempted but unsatisfactory on account of liquid feces obscuring the field, February 28th.

Rectal examination reveals a mass high up in the right anterior region. *Proctoscopy* reveals pus coming down, probably from an abscess on the right anterior region above the peritoneal reflexion. Suggest Barium X-ray. March 3rd.

Diagnosis: Diverticulitis.

Roentgenographic examination of the colon, March 7th.

The enema extended upward into the colon to near the hepatic



Figure 1—Barium enema showing multiple diverticula and a large abscess in the midline, resulting from diverticulitis.

*From the Department of Proctology, New York Polyclinic Medical School and Hospital.

flexure. The colon was very spastic and received a relatively small amount of barium. A number of diverticula is distributed on the colon. *A small quantity of barium suspension escaped into a sinus near the median line anterior to the upper segment of the sacrum. Just in front of this sinus there is a rounded cavity 3.5 by 2.5 centimeters in diameter.* (*Figures 1 and 2*).

After evacuation there was a very small colon residue and the quantity in the above described accessory cavity was decreased.



Figure 2—24-hour plate (prone) showing barium filling abscess in midline and also multiple diverticula.

Diagnosis: Old diverticulosis with probable subsequent diverticulitis and abscess formation which abscess has perforated into the colon. One accessory, round cavity has a contour suggesting that it may be lined with mucous membrane.—A. J. Quimby, M. D.

A cystoscopy was done and the report was negative, March 9th. The patient was referred to Dr. Lynch's Service for operation.

Operation, (by J. M. L.), March 10th.

Under general anesthesia a left lower rectus incision was made; peritoneal cavity was opened. About the bifurcation of the aorta, a heart-shaped mass could be outlined which was bound down by adhesions and fixed to the posterior peritoneal wall. This mass was soft and no attempt was made to disturb same because of the history of the case and the roentgenographic examination. It was thought best in view of the diverticula and the abscess to perform a temporary colostomy. Same was done at the mid-portion of the transverse colon.

The frequency which urinary symptoms occur in cases of diverticulitis has been overlooked. Mr. Hugh Lett, in a discussion on "Urinary Complications of Diseases of the Large Intestine," (the proceedings of the Royal Society of Medicine, London, October 1932) reviewed the records of 172 cases of Diverticulitis, admitted to the London Hospital during 10 years (1922-1931). Urinary symptoms, secondary to diverticulitis, were present in 17 or 10%. Temporary and slight disturbances of micturition may occur in cases of acute diverticulitis in which no abscess can be detected on clinical examination. Mr. Lett ascribes the urinary symptoms as being due to a direct involvement of some part of the urinary tract, either by the spread of inflammation, by adhesion, by invasion, by growth or by fistulous communication. The kidneys rarely are implicated, due to the protective barrier of fat and fascia.

The striking point in the foregoing case is that this patient's symptoms before admission to the hospital, were all referable to the genito-urinary system. Not until he took an enema did a train of symptoms start which pointed towards pathology of the gastro-intestinal tract. Such anomaly was proved by proctoscopic examination and roentgenographic study. Exploratory laparotomy confirmed the pre-operative diagnosis.

Following operation the patient had daily colonic irrigations through his colostomy with either normal saline solution or potassium permanganate 1-10,000. Four weeks after operation another Barium enema was administered and the roentgenographic plate as shown displays the complete disappearance of the abscess. Doctor Quimby reports the following—Barium was distributed through the colon from the transverse portion to the rectum and entered numerous diverticulae. The plate is negative for evidence of infiltration of the enema into the surrounding structure. The present finding indicates obliteration of the abscess cavity. (Figure 3.)

The patient left the hospital on the fifth week feeling extremely well. He is to return in about one month for closure of his colostomy, if he is symptom-free.

The lesson to be learned from this case is that when an acute pathologic process is present, surgically, the best procedure is to make a stoma cephalad to the site of the pathologic change and always at a sufficient distance so as not to



Figure 3—This plate was taken four weeks after colostomy. It reveals obliteration of abscess.

interfere with subsequent surgical intervention. When there is a fistulous opening into the bladder, it is better to allow the colostomy or stoma to remain open for a long time, in the hope that, if the current is side-tracked and the source of infection is eradicated, the opening into the bladder will close up. It is never safe to try to close the opening until all the inflammation has subsided. If it does not close of its own accord, an attempt may be made to close it afterward.

SECTION VIII—*Editorial*

The editorial contributions published in this Journal represent only the opinions of their writers. Such being the case, this Journal is in no way responsible for editorial expressions.

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

HIGHER EDUCATION AND "THE SLUGGISH SYSTEM"

The door opened. Our Secretary said "Miss Wilkerson[1] to see you on a personal matter."

There entered such a vision of young feminine pulchritude, so quietly, yet daintily clad, that an emotion possibly a bit deeper than demanded by the requirement of courtesy, brought us promptly to our feet to greet this late afternoon sunbeam. We clasped the hospitable, elegantly-gloved fingers which were, however, extended but a short distance and at the level of the fourth thoracic vertebra.

Having been seated, this in-that-early-twenties *charmer* flashed what to an Oldster bore qualities of a come hither look, the violet eyes—made up like those of the glorious gals who grin seductively from "Photoplay's" shiny front-cover—swept our sanctum, rested abruptly upon a football squad-picture and in dulcet tones—(the most approved Londonese modified *via* Boston)—emoted "Ah! *Dear* old Princeton! How oft, as a Wellesley girl, I have spent *deliciously* marvellous week-ends at Ivy! *Which* dear boy *is* your Son? Surely, I have *met* him! Few of the 'Big Four' boys are strangers to *me*!" etc., etc.—until our fixed stare at the clock checked the gushing outburst:

"The personal matter," recited most charmingly, frankly and with appropriate gestures and accompanied by discreet exhibitions of superbly-silked ankle and calf, briefly was: Doctor, you are *so* famous in your specialty and *so* widely known ("original research" to us!) that my employers, "The Butcher's Yeast Company," has selected you from simply *thousands* of specialists (!) for an *award*. (The trace of Scotch blood in our veins agitated our platelets mightily here!). As a *specialist*, you must know that most modern people, due to faulty food, lack of exercise, the daily "grind," worry, anxiety (and so on, *infinitum*), *actually poison* themselves *every* day in the *year*. Their "sluggish systems"—and *dear* Doctor, even men in your own profession are not exempt!—cause bad taste, *horrid* breath, headache, lack of appetite, easy fatigue, inability to concentrate, inefficiency (here a condemning "straight-eye" at *us*!), inferiority complex, nervous irritability, chronic dyspepsia, blotched and sallow skin, anemia, lack of "vital tone" (*did* her toe touch our shin?), complete psychic and physical disorganization and ultimately—*failure*!! Undoubtedly, "the sluggish system" caused the 1929-30 economic *debacle*, as these graphs demonstrate (here some fair replicas of brokers' charts) and, unquestionably, until "sluggish systems" are reduced to the *minima*, our wonderful country—in fact, the *entire world*!—can never rescue itself from the perfectly *dreadful* depression into which it has been plunged! Now, *dear* Doctor, the most renowned scientists of Europe have *proved*, by extensive experiments, that the *only* way to combat "the sluggish system" and thus bring health and harmony into *individual* and *national* life, is by the *regular eating of fresh yeast*—and, of course, *dear* Doctor, that means, really, "Butcher's Yeast," the yeast manufactured by my employers!—(here, a pause for breath and opportunity to draw a bit closer to us so that the next effort would appear more confidential: also, that we might scent the delicate odor of *Vol de Nuit* and have a few more volts and ohms from the flashing, violet eyes).

So, *dear* Doctor, although, as you can judge, I am not a *trained* scientist, my employers have commissioned me to secure from you a few words telling how, from your perfectly *enormous* and perfectly *wonderful* experience, you have prescribed yeast—particularly *our* yeast—to combat the poisons due to "the sluggish system," to energize and revitalize poor unfortunate sufferers. Of course, my *dear* Doctor (come hither look and the other "business" working overtime, now!) no one more than my employers and I *realize* how *enormously* valuable is your time (*this*, in the year of most acute economic paralysis!) and how *long* it will take you to *study* your *records* of patients: so, in order that you may not think that we plan to impose upon your philanthropic *spirit* and your professional *knowledge*, I am empowered to defray all the expenses of your research, *even* though the cost of your investigations may be as great as one thousand dollars! (Joyous visions of a new, shiny "Cadipack" invaded our frontal lobe; transiently only, we vow!). No! No! this must not be looked upon as a *fee*, merely, an "award," a slight and just compensation for your efforts in our behalf so that we may carry an authoritative message of cheer and encouragement to that vast army of sufferers from "sluggish system" throughout the world! European "specialists" have been *so* helpful! From France, Germany, Great Britain, the Scandanavian countries—in fact, from *all* the great centers of science in the Old World—we have secured the co-operation of the *very greatest specialists* in our campaign to rid the world of its greatest handicap: "the sluggish system." *Now* we are seeking the assistance of our *own* country's Great Specialists. Only a dozen are to be approached. But *these* men represent the very Flower of the Profession, the—(here about five hundred words extolling the virtues and accomplishments of "the holy dozen"—*us*, especially!).

Naturally, such outstanding men are somewhat timid with regards publicity, but you know, *dear* Doctor, times have changed: *now*, physicians feel that it is *really* their *duty* to enlighten less fortunate laymen respecting their ills and how to combat them by simple, basic, what may be termed, "household remedies." Even the management of your profession's most widely circulated magazine approves of and instructs the public generally about "household remedies," and I feel sure that it would not fail to emphasize the value of the regular and continued use of fresh yeast! Undoubtedly, when once a few men of *your standing* have certified our *quite* altruistic campaign and have permitted us to quote the results of *their* studies, it will not be difficult to enlist the support of other such Specialists as we chose to invite (our ears cocked up here!).

In fact, *dear* Doctor, in order not to take too much of your time, for purposes of brevity and so that announcement-schedules may be not disturbed, our Investigation Department has surveyed the entire field and summarized matters so that all now necessary is that you read over these statements (a batch of typed sheets, here, gently placed on our blotter, while an Eleanor Holm-like figure—quite unintentionally, *of* course!—brushed our right shoulder). As you see *instantly*, our Scientists have included, with astonishing clarity and comprehensiveness, don't you agree? (I did), everything that pertains to the significance of fresh yeast towards "the sluggish system." In order to obviate a lot of technical detail—you know, *dear* Doctor, the publishing business is just *choked* with *stupid* technical stuff!—you may select the "Research Summary" which most is in line with your own *vast* experience, sign your approval and thus avoid a *terrible* batch of dry, time-taking correspondence. If, *after* you have completed the study of your *own* patients' records, you find that your researches *add* to what our laboratories have discovered, you need simply forward to us the new facts. You have no idea with what consideration these facts will be received and how carefully—as your *very own* contributions, to which, naturally you are entitled to *priority*—they will be preserved in our files over your signature! If your experiments do *not* uncover facts differing from those included in *our* Scientists' summaries (these great, palisade-foreheaded

1 The experiences below detailed are not fanciful. They synopsize an actual occurrence. The names are substitutions.

lads unnamed so far as our gaze could determine or from the conversation of the fair Sybil from the yeast vats!). *This* is where you sign, *dear* Doctor. How *fortunate* it is that the *one signed check* which my employers are suggesting that I award you, merely as an honorarium, of course, is for as much as *one thousand dollars*! One cannot estimate accurately, of course, the cost in time and effort, of you and your assistants while making your investigations, but I can assure you, *dear* Doctor, that should this award not quite *cover* those costs, my employers will look leniently upon any additional statements you may render.

And speaking of photographs (had we dozed while the smooth, oh, so smooth, Miss Wilkerson, had been speaking: *positively* we had *not spoken* of any photographs!)—here a glance at the Princeton football huskies—hasn't your Secretary *just a "snapshot"* of you, as you work in your laboratory or at the hospital? One where you wear a white coat or gown and when you are deeply interested as you work out a knotty problem at the microscope or in the X-ray Department? I'd just *love* to have such a photograph for my *own* private collection (here, more high-power with the violet eyes!) and I'm sure that, in our announcement of your great discoveries upon the effects of fresh yeast in combating the horrid results of "the sluggish system," your photograph will carry conviction and authority to those whom all of us are trying to help! And, *dear* Doctor, I am sure that *you* will not consider *me bold* when I say that you *do* photograph most impressively! (*We*, whose family constantly remark upon our being pretty "moth eaten!").

Just glance at these replicas of some of the *distinguished* Continental Scientists who have joined our crusade against "the sluggish system:" Prof. Adolph Grabgeld, the famous, temporary, seventh Assistant *Docent* to the Dispensary of the Krankenhaus fur Reichsmarklos Wienerwurst Gestoffers in Bodenbach; Dr. Louis de Francboi, late Assistant, during the *summer semester*, Hospital de pitie de sujects, Hotcha sur Marne; Sir Whynot Bluffem (pronounced, "Chumley Haw-Haw!") Junior-in-charge, Hospital for Sick Ex-Scotland Yard Arab Scouts, Nettlesdew-on-Humber; Dr. Basilstein Roublehoarderwitski, Special Consultant in Blackbreadworm Diseases, Nova Novgarod; Dr. Gulpa Sphagetti, Chief of Staff, Hospital for Organ-grinder's Monkeys with Bunions, Amat-on-the-Tiber; Dr. Baron Janos von Koranalopo, eminent investigator, "Shrine of Health," Tetchen, Austria; Dr. Karl Aquavitson, renowned Swedish *ex-diener*, Pest-House, Upsala; Dr. Igotit Toto, world-famous Japanese research scholar, Imperial University of Tgsuri and—but our interest flagged on observing that several of the "stars" peered through 'scopes lacking slides on their stages and at least one "expert" intensely studied an upside-down X-ray film!

Our Sunbeam paused. With the "count at nine" on us, we managed to gasp: "But, Lady, aren't you in the wrong shop? We have a lot of doubts as to the frequency and the evil effects of "the sluggish system;" we aren't so keen a yeast-feeder as one might think; besides, broke tho' we may be, the Butcher Boys' cheque leaves us cold; why pick on us?—and, moreover, already, we're late for dinner"!

Wellesley gal or no, we up and fled. What became of our charmer we have no means of knowing.

But the end was not yet: Higher Education still pursued. At dinner we tuned in for what we hoped would be a much-regarded, string quintet. Instead, our dinner table was invaded by "the sluggish system" (nasty persons!) *via* Yale's urbane, but adenoidic, sinus-foggy, "crooner." Then followed an M.D., whom Harvard honored with a diploma and who became a "health authority," altho' no records exist of his ever being engaged in aught but commercial labor. This ballyhoo was "*toned for refined ears*," yet not toned *so* completely as to fail to instill the heebie-jeebies of "the sluggish system" into the minds of those who had barely "passed sixth grade," hence, still take seriously all folks who have traversed Harvard's sacred Yard. Simultaneously with dessert, there intruded the rather bored, "we-the-peepul"-voice of the Senior Senator from Megalopolis, a male, graduated by the long-defunct, politically-established and maintained Homeopathic Department of a distinguished Mid-Western University—a nose and throat surgeon by trade in the days when he worked for a living, but within a decade, a self-styled, self-propagandized, highly-touted, "world-famed Health Authority." General and inane were the words from this very "fountain-head" at Washington, but did they fail to saturate our dinner with the evils attendant upon "faulty elimination" and "the sluggish system?" They did not: though very discretely (since the noted Megalopolis' Senator is politically hitched with a major Brain Truster on a "Food and Drugs' Bill") the supreme value of yeast as a corrector of all human ills only was hinted at.

"What a program! What an intellectual trio! What a slam!"—doubtless gleed the sponsors of this hour of radio propaganda and entertainment. Could the combination be beaten? It could not—certainly, not for its cost!

Unquestionably, yeast and "the sluggish system" were being put over on the populace; "and ketch 'em when their eatin'! They *gotta* take it: don't every wun *eat*? I'll say! An' when they eat, don't they think of their bowels? They *do*? If they don't, *make* 'em think! That's good business: they begin takin' "our product," forget what a *natural* B.M. is *like* and when they *have* one, "our product" gets the credit! The "psychos" on our Advertising Staff have swell graphs shown' just how good a guy feels when he visions a "grand" B.M. An' them college fellers is *smart*, I'm sayin'! Didn't that gent what thought up "sluggish system" for a slogan, graduate from a college, an' didn't he get a whale of a "raise" when he sprung it! Why you ken use *them* polite words *anywhere:* them's *parlor words*, what could only be born from a feller whose been to college!"

"O, tempora! O, mores!"

However, being but a humble physician, we can but wonder how great is the harm accruing from the dozen or more radio broadcasts which teach false slogans regarding the effects of so-called colon stasis (elegantly, "the sluggish system!"); which influence quite normal folk towards developing habits of constantly interfering with adequate digestive sequences; whose sponsors seduce, by heavy subsidy, men in the public eye to broadcast on topics about which they have no special knowledge; which, for commercial gain, are willing to frighten out of their wits by lies, half-truths and fake "cases," half our adult population; which frankly *buy* favorable statements from *less than ordinary* doctors and then palm off on the public such professional renegades as being outstanding scientists or clinicians (which they *well know* is *not* so even when they announce the "eminents' " names and print their portraits!); which sponsors annually take millions of dollars from the pockets of dupes and, by the furtherance of self-medication, yearly rob thousands of the really ill of their opportunities for help at a time when help could be given.

Recently, the Council of the Chicago Medical Society moved to condemn the radio-broadcasting of "medical or therapeutic" advice by unqualified or unauthorized persons or firms. Such action, decidedly, is a step in the right direction; but the effect of the Society's petition doubtless, will be *nil*. When one hears, *via radio*, pseudo-learned discussions of "the sluggish system," yeast and other cure-alls, one does not hear the voice of authority: it is *money* which is talking, money which aims to grow bigger—and talk louder—by attracting more money from those whom it fools.

Meanwhile the "nutrition" lads and the "vitamine" boys fiddle with foods and animals, collecting ammunition later to be employed, by certain of the commercial houses which *hire them*, to trick the public, to interfere with the legitimate practice of medicine and to bring false hope to folks who may be dangerously ill. Is there no *quota* set to limit the output of potentially harmful agents or to the number of words howling their fancied virtues through the ether? F. S.

SECTION IX—*Book Reviews*

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

This Journal is not responsible for the opinions, decisions or grouping expressed by reviewers of books or pamphlets. For the guidance of readers, an attempt is made to indicate the relative worth of reviewed material by placing "stars"— in connection with the reviews. The greater the number of "stars," the more agreeably and importantly does the book or pamphlet impress the reviewer.*

* * * * *Die Hormone.* von Paul Trendelenburg and Otto Krayer. Published by Julius Springer, Berlin, 1934. 502 pages.

A very complete and up-to-date survey of the subject of hormones.

This work was started by Prof. Trendelenburg, but due to his death had to be completed by O. Krayer, professor of pharmacology at the University of Berlin. The survey covers: Thyroid, 221 pages; Parathyroid 72 pages; Pancreas 150 pages; Thymus 20 pages; Epiphysis 13 pages.

A very complete survey of the literature and 62 cuts accompany the text. The authors have combed the world literature on the subject and have presented a complete and up-to-date digest of this material. The book should be a valuable adjunct to the library of students of endocrinology.

Henry J. John

* "*Modern Aspects of Gastro-Enterology*," by M. A. Arafa—M.R.C.P. (London). Med. Assistant to Guy's Hospital, London; Med. Tutor to the Egyptian University and formerly Senior Medical Registrar to Kasr-El-Ainy Hospital, Cairo; foreword by Arthur F. Hurst, M.D., F.R.C.P., published by Bailliere, Tindall & Cox, 7-8 Henrietta Street, Covent Gardens, W. C. 2.

This book is the work of an enthusiastic student of Sir Arthur Hurst, who sponsors the publication with a laudatory introduction. This is as it should be, since the entire book is replete with the observations, opinions and criticisms of Sir Arthur Hurst, himself. As a matter of fact the title of the book appears to be a misnomer, for it might have been published more accurately under the title of "Recent Expressions in Gastro-Enterology," by Sir Arthur Hurst.

The entire book is written down to the level of the second or third year medical student. The first chapter reads like a beginner's course in general medicine giving, in detail, the value and method of taking a history and of the physical examination of the patient. Even in this elementary introduction, the enthusiasm of the young author, worshipping at the feet of his god, runs away with him, for in a discussion of dysphagia as a *symptom*, we find an entirely irrelevant and detailed discussion of the value of the Hurst mercury tube in the treatment of achalasia of the cardia.

The continuity of this fundamental course in medicine becomes uneven in Chapter 2, the first part of which deals with the radiology of the stomach and intestine and is poorly written and very incomplete. The latter half contains an excellent description of the various methods of gastric analysis.

Starting with the third chapter, the author opens the discussion of various gastro-intestinal disturbances by a description of chronic gastritis. A critical analysis of this chapter reveals an enthusiastic eulogy on the Sir Arthur Hurst's method of cure by gastric lavage with hydrogen peroxide; no other form of treatment, apparently, being worthy of consideration.

Yet, it is in the next chapter that your reviewer is fed with the doctrines of Hurst, *ad nauseam*, for the author heads his chapter on the therapy of peptic ulcer, as follows: "The present regime of adequate medical treatment (of peptic ulcer) owes its perfection largely to Hurst and his co-workers." In the event that any criticism of exaggeration may be levelled at this comment, let this reviewer add a few more quotations. The author tells us that the most important factor in the pathogenesis of ulcer is, as Hurst says, the "hypersthenic gastric diathesis;" that the only role which surgery plays in the treatment of ulcer is, as Hurst says, "an incident in the medical treatment." There are many other examples of "Hurstiana," including the characteristic method of dividing peptic ulcer into only two groups, either "acute erosions" or "*chronic*" ulcer.

In a chapter headed "Investigation of Intestinal Disease," the author reaches his best work of the book. A carefully written and lucid description of the value of the analysis of the feces affords excellent reading and is replete with many pertinent observations. This chapter is enriched by several well illustrated plates of the elements of the feces, as well as by some excellent colored plates of the colonic lesions of amebic dysentery, bacillary dysentery and other tropical diseases. Many of these are reprinted from previous work by Biggam and Arafa.

Just as this part of the book represents the high point, the remainder sinks rapidly into a confused and vague latter half. The chapter on "Cholecystography" is a brief summary of previous writings and contains only two illustrations. "The Examination of the Duodenal Contents" is a chapter added by Dr. F. A. Knott of Guy's Hospital and is but a short *resume* of previous publications by other authors. Next comes the chapter dealing with the pancreas which seems to be written hastily and adds nothing of any value to what has been published in many books long since classified as obsolete.

In the chapter entitled "The Simulation of Gastro-Intestinal Diseases," the author demonstrates the inadequacy and the limited scope of his experience, especially in dismissing the large group of functional nervous conditions with but a passing note.

The last chapter, "Practical Dietetics," portrays the enthusiasm of the young student again, for here one finds more than four printed pages of detailed discussion of the Hurst *regime* in the treatment of peptic ulcer, whereas but eight pages are given to the relation of diet in *all other* diseases pertaining to the gastro-intestinal tract.

To inspire a post-graduate student, particularly a wanderer from distant Egypt, awed by the old-world grandeur of London, is unquestionably a fine thing; to send him back home enriched by study and association of many months, is certainly a commendable piece of work; but all this is still not reason enough for the publication of an amateurishly written, incomplete book which praises the *dicta* of the one teacher to the exclusion of the mature observations of the medical world.

Specifically, criticism is directed to the meager illustrations, many of them not original; to the short and totally inadequate chapters on therapy; to failure to give recognition to the value of the X-ray in diagnosis and to the absence of the discussion, as separate entities, of such important disease groups as syphilis and tuberculosis of the gastro-intestinal tract, and to the non-specific granulomata and lesions of the small intestine.

As a quiz compendium to a course in gastro-enterology by Sir Arthur Hurst, this volume may be very valuable, but it can never hope to find an equal footing with many excellent books on gastro-enterology already published and readily available.

Martin G. Vorhaus.

Gastric Anacidity: Its Relations to Disease. By Arthur L. Bloomfield, M.D., Professor of Medicine, Stanford University, San Francisco, and W. Scott Polland, M.D., Instructor in Medicine, Stanford University, San Francisco. The MacMillan Company, New York, 1933. Price, $2.50.

This book containing 188 pages, presents in a concise manner the important facts gleaned from the mass of literature on gastric anacidity. The authors have sanely analyzed the older literature in the light of modern knowledge and have pointed out many misconceptions that have arisen. Much of the material in the text is derived from their own published papers and their own experience. The advantages of the standard histamine stimulus and the importance of comparing the percentage of anacidity found in various disease groups to the incidence of anacidity occurring in the corresponding normal age groups are pointed out clearly. In discussing the terminology of gastric anacidity the term "true anacidity" is introduced to define the condition in which both acid and ferments are lacking after standard histamine stimulus. The etiology, pathogenesis, and clinical features of anacidity are fully discussed. Those chapters devoted to false anacidity, the anacidity observed in pernicious anemia and cancer of the stomach, and the association of anacidity with a wide range of other clinical conditions, make the book particularly valuable to the gastroenterologist and internist. The chapter devoted to prognosis and therapy of anacidity is based on sound medicine.

The book contains references to 272 papers with a comprehensive author and subject index. Graphs and tables have been employed unsparingly throughout the text. It is distinctly a valuable summary of the work on gastric anacidity.

Oscar M. Helmer.

**** *Gastric Anacidity:* Arthur L. Bloomfield, M.D., and W. Scott Polland, M.D. The MacMillan Co., New York, N. Y., 1933.

For several reasons this is the most satisfactory monograph on the subject of gastric anacidity: it is the latest, and therefore has the advantage of a complete review; the arrangement of the book is highly gratifying; finally, the authors write from a long, and very close practical acquaintance with the subject, and not from second-hand sources.

The need for this book is obvious. The average internist has the habit of ordering gastric analyses on most of his patients with digestive symptoms and he will therefore be in a much better position now to adopt an intelligent viewpoint with regard to achlorhydria when he discovers it. Perhaps he will tend to lay less stress than formerly upon the significance of gastric anacidity, but, at any rate, he will have no excuse for magnifying the condition beyond the limits of importance which Bloomfield and Polland have fairly set.

The most fundamental point in practice is that the test of gastric acidity be carried out with the histamine technique, because this method only gives reliable results and because in the future, reports using other methods, such as the test-meal, will be granted little credence. As a concession to custom, perhaps it is wiser to give a test meal along with the histamine injection. Test meals alone (Ewald, gruel, etc.) do not furnish a stimulus sufficiently powerful to bring out the full, or latent capabilities of the secretory mechanism, and therefore false anacidities will be found. Other points, such as preliminary gastric lavage, and the ordinance of basal conditions, are of such importance that, before carrying out a series of tests, the practitioner ought to adopt the full ritual or else not be too sure of his results.

Di-methyl-amino-azobenzol (Topffer's reagent) is fairly reliable as an indicator for free acid; but since the color change occurs at pH 3.0, there may be a good deal of acid masked by buffers contained in the test-meal or in gastric mucus. By adding alkali, and titrating the combined acid thus liberated with phenolphthalein, a rough estimate of this "combined acid" may be obtained. But this reading of "combined acid" may be nothing more than a reading of the buffer capacity of the mucus, and it does not positively indicate that any acid has been secreted.

Historically, as is well known, the anatomic and histologic leanings of the physicians of the last century, combined with their lack of emphasis on functional tests, with a few very brilliant exceptions (Beaumont especially), lent a confusion to the whole subject which is still not entirely dispelled. Much of the "gastric atrophy" reported was due to uncontrolled post-mortem changes. Faber's formalin fixation method did away with many reports of "atrophy," but also brought to light evidence of "gastritis" in association with achlorhydria. Faber, and others viewed the gastritis as being the cause of the lack of acid secretion. The other school, led by Martius and supported chiefly by Hurst, regarded achlorhydria as a constitutional anomaly, congenital, and even hereditary. This would serve a most convenient argumentative requirement, and permit us to view the gastritis as secondary to the achlorhydria except for the emergent fact (and this is one of the chief contributions of the present volume) that a close study of recent reports on the age incidence of achlorhydria (determined, of course, by reliable technique) certainly do not support the idea of anacidity being a congenital anomaly. On the contrary, it appears to be rather "the playing out," as time goes on, of a phylogenetically recently acquired function of vertebrates. This attitude, born of hard-headed deduction, should now displace all previous conceptions, born of endless theories, and it leaves us, temporarily, in a greater quandary than ever, especially with regard to the etiology of pernicious anemia. Whether a definite distinction among the terms anacidity, achlorhydria and achylia gastrica ought to be made seems uncertain, although Helmer, Fonts and Zerfas[1] suggest that "achylia gastrica" be reserved for cases in which not only acid and pepsin and rennin are absent, but also the intrinsic gastric factor of Castle.

The finding of clinical pernicious anemia in occasional persons with free acid secretion but without the intrinsic factor of Castle, directs attention to the absence of this factor as the essential etiological process, but the disturbing fact that 2 or 3 cases of persons with no intrinsic factor of Castle, have refused thus far to develop pernicious anemia, throws us temporarily upon the conjecture that the absence of the intrinsic factor is only one requirement in the pathogenesis of this most baffling condition.

Anacidity seems indeed to be a permanent condition, with the possible exceptions of a few cases of improvement and return of function in alcoholic gastritis, after cessation of the abuse of alcohol. "Unexplained anacidity" is suggested as a term to cover all the many cases of truly proved anacidity in persons clinically free of disease. Familiar anacidity may be more apparent than real, since, mathematically, with recent statistics in mind, *the chance that there will be two or more cases of anacidity in a family of four is 27.4 in 100.* The cause of anacidity is at present unknowable, unless we adopt the view that it is due to the cessation with age of a function of vertebrates rather recently acquired.

A gastritis usually is associated with it. Thus far, only one case of thoroughly "pedigreed," true, unexplained anacidity has come to autopsy, and reliable histologic technique here demonstrated a picture that might be called "anaplastic" with some evidence of mild inflammation. Certainly, the gastritis cannot be regarded as causing the achlorhydria. It may transpire that, once the acid secreting function has "played out" in a given person, that the gastric mucosa, robbed of its normal antiseptic weapon, succumbs to the combined insult of hard, insufficiently macerated food

1 O. M. Helmer, P. J. Fonts, L. G. Zerfas (Gastro-intestinal Studies: IV. The Relation of pH to Pepsin and Rennin Content of the Gastric Juice; *Am. J. Dig. Dis. & Nut.*, I, 2, April 1934. 120-123.)

roughage and the ingress, through local points of injury, of pathologenic mouth organisms swallowed in the saliva.

Perhaps the stomach of man, and dogs as well, is a less important organ than imagined. Certainly, the absence of the organ causes frequently no inconvenience of note, provided the operation of total gastrectomy is "successful." Anacidity really does *not*, in itself, regularly disturb gastric or intestinal motility. The "gastrogenous diarrhoea," at least in pernicious anemia, rapidly subsides on treatment with liver extract alone, and also in healthy individuals by such common-sense measures as bland diets and rest, although it is admitted that HCl very often has an apparently beneficial effect.

Recently Bloomfield did much to smash the "hypochromic microcytic-anemia-with-achlorhydria" syndrome of modern writers and we think he deserves praise in this connection, for the idea can scarcely stand scrutiny. When it is remembered that there are probably a thousand possible causes for clinical anemias and that, actually, aside from anemia due to hemorrhage, we know little regarding their etiology, it will be seen how easily false entities may be constructed unless the logical methods of the present authors are employed.

Lessened acid secretion or actual total anacidity may, and frequently does, accompany gastric carcinoma in varying degrees; is always associated with a gastritis of varying extent and is, in all probability, due to this gastritis. The main problem is whether or not the carcinoma results from the gastritis. The answer probably is in the affirmative.

On the whole, anacidity in otherwise normal persons is a pretty harmless affair, except that it is from the ranks of these persons that cases of pernicious anemia and gastric cancer are most liable to be recruited. Perhaps persons with anacidity are slightly "less normal" and robust than others.

Is any treatment needed for the patient, for his anacidity? Certainly, *focal infection should be surely eradicated*, especially pyorrhoea alveolaris, in an attempt to lessen the associated "anatomical gastritis;" the use of dilute HCl often seems to help symptoms if such be present; general measures, such as physiotherapy, are as advisable as if the gastric secretions were normal. Finally, and on this point many readers will agree, the use of liver or liver extract frequently appears to be of decided benefit, and is quite justifiable as a trial measure, particularly if *any type* of anemia or, in fact, any kind of disease (other than polycythemia) be present, but there is no known assurance that such treatment will ever bring about normal gastric acidity.

Beaumont S. Cornell.

**A new approach to dietetic therapy in Epilepsy, Eclampsia of Pregnancy and Infancy, Migraine, Angina Pectoris, Bronchial Asthma, Allergic Diseases, Gout, Essential Hypertension, Pernicious Anemia, Polycythemia, Acne Vulgaris, Nervous and Psychic Disturbances, Constitutional Changes, Aging, etc. Metabolism of Water and Minerals and its Disturbances. By Eugene Foldes, M.D., Formerly Assistant Professor of Medicine, University of Budapest, Hungary. 1933. Boston: Richard G. Badger. The Gorham Press.

This book deals with certain basic principles and fundamentals of the relation of human water and mineral metabolism to disease and diet.

The author propounds new questions and aims at the solution of these by disclosing the physical and chemical phenomenon of the cell. He discusses the relation of these factors between the blood and the various body fluids, between the blood and the intercellular fluids and lastly between the intercellular and the intracellular fluids.

While many theories which he presents are not even in the realm of fact yet the evidence which he presents to support these theories often is quite convincing.

The entire book emphasizes the metabolism of water and inorganic substances, rather than upon the organic, and every effort is made to demonstrate that the impairment of this metabolism plays a major role in the pathogenesis of the diseases outlined in the title of the book. With this conception he proceeds to point out the therapeutic relation of diet to disease by its influence on the water and mineral metabolism.

The studies of water and mineral metabolism have been focused upon visible edema, but in this treatise the clinical significance of the visible edemas are surpassed by non-visible retentions.

The author states that the stomach and upper portion of the small intestines play a role in the water and mineral metabolism next to that of the kidneys. The mucous membrane permits the passage of chloride and H ions from the blood to the gastric contents until an equilibrium is established. The presence of HCl in the stomach is explained on a physiochemical basis rather than on the assumption of a mysterious vital secretion. Accordingly, a hyperchlorhydria is not due to a "secretory disturbance," but to an increased concentration of acid substances in the blood. The gastric juice may be looked upon rather as an excreta, serving the regulation of the acid base equilibrium.

Two kinds of disturbances of the water and mineral metabolism are met with particularly in the above mentioned diseases and pathological conditions: (1) General retention of water and minerals and (2) mobilization and consecutive local accumulation of water and minerals previously retained throughout the body. The circumstances which account for that which is common in all of these diseases, i.e., the development of retention or mobilization of water and minerals, are discussed in the first part of the book. Practically all phases of the general water and mineral metabolism, as a single unit, are considered except those related to the genesis of visible edemas.

The first part bears the title "Physiology and General Pathology of the Water and Mineral Metabolism." The second part of the book discusses the special pathology of the retentions and mobilization of water and minerals in each respective disease, making each disease a distinct pathological entity despite the similar disturbances of the water and mineral metabolism in all of them. The third part presents the therapeutic conclusions and the results obtained in the treatment of patients.

The writer considers nutrition as the best possible method of an anti-retentional treatment. There are certain factors of a diet that have a very effective diuretic influence on the organism while others have a definite retentional influence. Therefore the main principles to consider in an antiretentional diet are (1) to select food substances that have antiretentional action and restrict those that have retentional action, (2) to supply adequate energy, as well as all accessory substance as minerals and vitamins and (3) to consider palatability and the avoidance of monotony.

The antiretentional diet is a high protein diet, on the basis that an increased protein metabolism influences water elimination.

The nucleoproteids are given special consideration because of their powerful diuretic action on the purin bases and to certain amino acids which seem to accompany nucleoproteids.

High carbohydrate diet produces a water and mineral retention, therefore their restriction in the antiretentional diet is necessary. The diet may contain carbohydrate from 2.5 gm. to 3.5 gm. per kg. of ideal body weight.

A diet rich in fats leads to water retention therefore the fat in the diet should not have more than 40 to 50 grams daily.

Restriction of salt is not necessary. Salt has a diuretic action if liquids are restricted. Liquids should also be restricted to avoid retention due to an excess of liquids. The antiretentional diet should contain an ample supply of minerals of vegetables, of fruits, and of animal foods.

Vitamins should be adequate in the diet but an excessive amount of vitamins must be restricted to prevent hyper-

vitaminosis. Also they should be considered in reference to their effect on retention and elimination of water.

The calories in the antiretentional diet should be low, just enough to meet the minimum needs of the body.

In other words the antiretentional diet should be arranged so as to give the highest amounts of proteins per kg. ideal body weight (between 1.5 to 1.8 gm.), large amounts of purin nitrogen (0.08 gm. or more), low quantities of carbohydrate per kg. ideal body weight (2.5 gm.), no visible fats and a daily liquid intake slightly above the minimum (3 glasses or 600 c.c. of water in addition to that contained in fruit and milk).

The author admits the utilizing of hypothesis to bridge the gaps that must of necessity exist when dealing with factors explained on the basis of physio-chemical phenomina of the water and mineral metabolism of the cells of the body.

Many parts of the book are open to controversies and considerable criticism while other parts are so illuminating and convincing that they are readily acceptable to the reader.

While the book is well written, full of theoretical ideas some of which may very likely yield valuable results, its attraction will be confined primarily to those interested in fundamental research.

Clifford J. Barborka.

Alimentacion, Libreria Hachette S. A., Maipu 49, Buenos Aires, 1934, 315 pages. Professor Pedro Escudero, Director of the Municipal Institute of Nutrition.

This study presents in Spanish an interesting summary of the relations of nutrition to the biologic and medical problems of a South American people. He gives a summary of the examination of 426,368 Argentine conscripts of whom 29 per cent were not fit for service. He points to the fact that in Buenos Aires the average expectation of life was but 38.4 years as compared with 49.0 years for New York in 1927. Other vital statistics such as the infant mortality and tuberculosis rates, are analyzed. He discusses the cost of an adequate diet and gives the average cost for adequate diets in the Municipal Hospital. Discussion of the pregnant woman in different periods of pregnancy is given much space, as well as the diet for workers with very limited income. Vitamines and the protein requirement are stressed. He stresses the importance of educating physicians and the public in the attainment of normal nutrition. Professor Escudero stands as one of the foremost clinicians and students of metabolism in South America. This brief book is well worth reading.

Howard F. Root

ABSTRACTS

SHAY, HARRY, M.D., AND SCHLOSS, EUGENE M., M.D.

With the report of a case of Ulcerating Carcinoma in which the gastric acidity changed from normal to anacidity while under observation. Annals of Internal Medicine, April 1934, 7:1218.

(1) One of every 20 persons dying after 10 years of age does so because of cancer of the stomach; (2) Cancer of this organ accounts for about one-third of all the deaths from cancer; (3) the incidence of cancer is on the increase; (4) XXXX, it is doubtful whether physicians see gastric carcinoma early enough to produce a cure in more than from 1 to 2 percent of the cases; (5) medical opinion at various times has considered gastric ulcer the precursor of gastric cancer in 60 percent or more of the cases.

These figures and viewpoints justify some feeling of pessimism. On the other hand, when it is remembered that in Gregory Cole's opinion simple gastric ulcer may readily be healed by medical treatment; that many of us believe gastric cancer is only seldom engrafted upon gastric ulcer; and that there are available certain criteria which may be applied over a reasonably safe period to permit a definite clinical opinion.

Historical evidence for or against the possible malignancy of an ulcerated lesion of the stomach may best be considered under the following headings:

1. Duration of symptoms. 2. Nature of symptoms. 3. Response of symptoms to treatment.

In gastric carcinoma a short history is generally obtainable; usually there is a history of gastric symptoms of less than a year's duration. It may, of course, be shorter or longer.

Evidence from gastric analysis, while important, is nevertheless inconclusive. In the authors' series of 53 cases, 36 had fractional analysis, of whom 16 or 11.1 percent showed anacidity; 11 or 30.6 percent showed a hyperchlorhydria; 6 or 16.6 percent a normal acid response; and 3 or 8.3 percent hyperchlorhydria.

Zenker first called attention to the persistence of free hydrochloric acid in the stomach contents in ulcer—cancer, it has often been intimated that such a finding in cases of gastric carcinoma points to an ulcer origin. Because of the short history of a year or less in six of the nine of the normal and hyperacid cases the authors' report, and because of the ulcerating lesion found in so many of their achlorhydric groups, plus the fact that the incidence of gastric carcinomas which showed adequate free HCl is entirely too high to be accounted for by the ulcer-cancer group, they are unable to subscribe to the above views. Of the numerous theories suggested to explain the relatively high incidence of anacidity in gastric cancer, that of an associated chronic gastritis appears most logical and receives the greatest support.

The authors believe that occult blood reaction in the stool, in differential diagnosis, can not be of much help unless it becomes negative and remains so. Occult blood in the gastric contents when found on repetition of fractional gastric analysis is of considerable value in differentiation. In the benign ulcer under proper medical treatment occult blood reaction soon disappears whereas in malignant ulceration the reaction continues positive. Roentgen-ray is of little help, the authors think, in our present problem because ulcer and cancer may both produce identical Roentgen signs. The location of the lesion is, however, of importance. The majority of cancers occur at the pylorus while most of the ulcers occur on the lesser curvature. The prepyloric ulcers show the greatest tendency to malignant change. The authors cite a case of carcinoma of the stomach under their observation showing free HCl in the fasting residuum May 29, 1931, and a complete absence of free HCl Dec. 4, 1931.

Allen Jones

SECTION X—*After "Hours"*

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not)

THE HISTORICAL AND BIOLOGICAL EVOLUTION OF HUMAN DIET*

By

SAMUEL S. ALTSHULER, M.D.

DETROIT, MICHIGAN

IN A DAY when advertising copy writers are bursting with information about the "balanced" diet, when every third billboard speaks sternly to us of our need for vitamins, for citrus fruits, for iron, phosphorus and calcium, sometimes it occurs to us to wonder how our grandparents managed to grow up at all, ignorant as they were of these facts of life. And yet our grandparents lived in the same kind of a world that we do. The dietetic possibilities open to them were substantially the same as are those which we face, and if they ate frivolously what tasted good instead of solemnly what "balanced" the diet the degree of error was limited.

How much more remarkable it is that *Homo sapiens* altogether managed to grow up! He and his *homo-simian* precursors adjusted themselves to a world in which the very flora and fauna were radically different from what we know. They survived glacial periods. They did without such comparatively recent innovations as agriculture and domesticated animals.

From the remains which these creatures—human and sub-human—have left, and from observation of recent and existing primitive cultures, we are able to trace the dietetic changes which took place during the prehistoric period of man's development.

It seems obvious that one of the very earliest variations between the creature which became man and the creature which remained ape was one of diet. Indeed, Carveth Read defends brilliantly an hypothesis that *all* differences between man and the anthropoids can be traced to man's adoption of a flesh diet and consequent assumption of the habits of a hunter.

The diet of the great anthropoids, with whom we presumably have a *common* ancestor, mainly is frugivorous. Though they are occasionally known to eat birds' eggs and young birds (the gorilla is said to eat small mammals, and other primates eat insects, crabs, worms and so forth), they depend for existence on vegetable food.

The teeth of the gorilla, most man-like of apes, closely resemble those of man in number, kind and general pattern of their crowns but they exhibit marked differences in relative size, in complexity and in presence of fangs. The teeth of man constitute a regular and even series without any break and without any marked projection of one tooth above the level of the rest, a peculiarity shared by no other living mammal. The teeth of the gorilla, on the contrary, exhibit a break or interval—termed the *diastema*—in both jaws; in front of the eye-tooth, or between it and the outer incisor, in the upper jaw; behind the eye-tooth, or between it and the front false molar, in the lower jaw. Into this gap in each jaw fits the canine of the opposite jaw. The size of the eye-tooth in the gorilla is so great that it projects like a tusk far beyond the level of the other teeth.

Man's earliest ancestor of whom we have any knowledge is *Pithecanthropus erectus* (see Table 1) who flourished about a million years ago. The remains of this creature were found in Java in a stratum generally considered to be contemporary with the First or Gunz glaciation in Europe, although some authorities have placed it slightly earlier. Java was at that time a part of the mainland of Asia. *Pithecanthropus*—he is not yet *Homo*, even nominally—left a straight thigh bone, indicating that he walked erect; he left a skull cap which shows his cranial capacity to have been about 900 c.c., halfway, that is, between a large ape brain of 600 c.c. and a small human brain of 1200 c.c.; and what is most important for the purpose of this paper, he left three distinctly human molar teeth. It is reasonable to assume that if the animal's teeth were not ape-like neither was his diet.

Again, with *Homo heidelbergensis*, whose age is estimated at half a million years, the teeth give us a clue of great significance. This race is identified with one find only—a lower jaw, the largest and stoutest human mandible known. This jaw shows an ape-like lack of chin, and bones close in upon the space left for the tongue to such an extent as to interfere seriously with the use of the tongue in articulate speech. Yet even here, in a creature so primitive that it possibly fell short of the universal human trait of speech, the teeth are distinctly human. The canine teeth, unlike those of the anthropoids, do not project beyond the line of the other teeth and therefore were not used as are the teeth of apes.

The Antiquity of Man

Culture			Man	Years
Neolithic and Modern			Living Races	10,000
Azilian			Transition to Modern	25,000
Paleolithic Age	Upper	Magdalenian	Cro-Magnon	
		Solutrean	Brunn (?)	
		Aurignacian	Grimaldi	
	Lower	Mousterian	Neanderthal	50,000
		Acheulian	Neanderthal (?)	100,000
		Chellean		
Eolithic			Heidelberg	500,000
			Pithecanthropus	1,000,000

Table 1

Thus from what we know of the teeth of his forebears, at some early stage in man's evolution there was a change in his habits of diet. From the gathering of fresh vegetable food as a sole resource, he turned to the hunting of flesh. The adoption of this diet made possible man's dominion over the entire earth. It freed him from tropical jungles, helped him to spread over the temperate northerly grasslands and was a material factor in his survival of the Ice Age.

The single exception to these observations on the teeth of prehistoric *homo-simians* is *Eoanthropus dawsoni*, more familiarly known as "Piltdown man," a find consisting of fragments of a female human skull of comparatively high cranial capacity together with a jaw bone which closely resembles that of a chimpanzee, especially in regard to the teeth. This, however, is one of the most disputed finds in all archeology. The bones were uncovered in a gravel pit in a stratum only a few feet below the surface in company with fossils which had been washed or rolled into the layer. Some of them are certainly much older than the skull, which in itself is not par-

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ticularly primitive except for unusual thickness of the bone. Many competent authorities have resolved the difficulties arising from this find by assuming the skull and jaw bone to have come from two different creatures: one contemporary and human, one ancient and simian. Since, therefore, the status of *Eoanthropus* is a matter of speculation and not of knowledge, the whole find need not be regarded seriously.

Our knowledge of the earliest culture of primitive man comes not from his remains but from artefacts which he left. Yet in strata pre-dating those in which there are known artefacts, flints have been found with rude cutting edges which may have been chipped by man or may have been so fashioned by accident of nature. It seems highly logical to suppose that there was a time when man made use of such stones as were of convenient size and shape before he ever thought of shaping them himself.

The name given to this most primitive of all periods of culture is Eolithic (Dawn Stone). Our knowledge about it comes largely from deduction and inference. There are no human remains identified with this epoch nor are the flints and other stones left such that they can be said conclusively to be the product of a purposeful intelligence. A single people, however, the Tasmanians, remained in an Eolithic state of culture down almost to our day and by studying them we can get an idea of how primitive men were living in Europe over a hundred thousand years ago.

The implements of the Tasmanians resemble flints of the Eolithic period so closely as practically to be indistinguishable from them, were they not made from a different kind of stone. Tasmanians have been known, when they needed a cutting instrument, to catch up a suitable stone, knock off chips from one side, partly or all around the edge, and to use it without further ado. They have done this under the eyes of modern Europeans.

The Tasmanians lived in hunting tribes. While they ate birds, eggs and shell fish, they depended largely on game. The animals that they succeeded in killing were roasted whole in the skin and cut up with stone knives. The ashes of the wood fire were sometimes used as a seasoning in the absence of salt. For vegetable food they had shoots of fern and bullrush roots.

These people did not use fish because they knew nothing of nets or fish-hooks. Cooking by boiling was also unknown to them. They did not, however, take kindly to instruction in these matters. Their ignorance of fish was safe-guarded by a solemn taboo and when introduced to boiled foods they did not hesitate to pronounce them unpalatable. They had no domestic animals, not even the dog.

The Tasmanians did have a sort of wine made from sweet juice of gum trees allowed to ferment. Apparently there were limits to primitive man's simplicity.

Men of the Eolithic period must have led an existence comparable with that of the Tasmanians. At least, we have no reason for supposing otherwise since they lived in the open and left no remains.

The first two periods of the Paleolithic Age—Chellean and Acheulian—are also without human remains, but the stone implements found are unquestionably the work of man.

The Mousterian period, however, saw the advance of the Fourth or Wurm glaciation. Man was compelled to seek the protection of caves and rock shelters, and here for the first time we are able to study early home life in Europe. The new conditions gave less freedom of movement. Man was still a hunter, but the number of natural shelters was limited, and, once a group was in possession, it apparently remained until dispossessed or until the exigencies of the hunt for food caused its voluntary movement.

During this period *Homo neanderthalensis* flourished, although he had almost certainly appeared earlier. From the score or more finds of this species that have been uncovered, we know that the men were about five feet three inches in height and the women were several inches shorter. They had long narrow heads with very prominent supraorbital ridges back of which the forehead retreated abruptly, indicating little development of the anterior portion of the brain, but the occipital region was so expanded that the average cranial capacity was around 1550 c.c. The *foramen magnum* was situated farther back than in modern man and this, together with the points of articulation of the skull with the bones of the neck, shows that the head hung habitually forward on the chest. The arms were long in proportion to the legs and in all cases the thigh bone was curved, which, considering the muscle attachments, indicates that Neanderthal man walked in a semi-erect position.

These small awkward people, with their rude spears and stone axes—they had not even the bow and arrow—lived on big game of a kind that modern men would hesitate to attack. The hearths of the Mousterian period reveal the bones of animals which had served as food. Among these the formidable cave bear is by far the most common. The wild horse and reindeer are represented as are also, to our awe and amazement, the mammoth, the bison and the rhinoceros. The bones of these animals are invariably broken open for marrow—a custom common to the entire Paleolithic Age.

It is interesting to note that this people, the first of whom we have any extensive knowledge, were familiar with the use of fire and were accustomed to cooking. Obviously at some time there must have been a pre-cooking era, but it was already remote when Neanderthal man crouched beside his hearth fifty thousand years ago.

For more detailed information about the customs and life of the Mousterian period, we turn to a study of the aborigines of Australia, whose culture provides a close parallel.

These people are, of course, hunters. They do not have the bow but their spears are superior to those of the Tasmanians. They fish both with spears and nets. Their meats are broiled rather than roasted. For vegetable food they have yams, a kind of truffle and manna. The seeds of certain plants are ground between stones into a coarse meal which is then made into a paste with water. This may be eaten raw or baked into cakes. The superiority of this culture to that of the Tasmanians needs no comment.

The close of the Mousterian period marks the end of the Lower Paleolithic Age. With Aurignacian times comes an abrupt and revolutionary change in methods of flint working and in the entire way of living. A new species of man has come into Europe, the first great race of *Homo sapiens*—Cro-Magnon.

While he was not the sole occupant of the continent—we know of two other races, Grimaldi and Brunn—he was dominant, and it is his culture which is typical of the period. It is thought that Cro-Magnon man probably underwent a long period of development somewhere in Asia and entered Europe with all his physical characteristics fully established. There is no reason to consider him as a development of, or closely related to, Neanderthal man. He appears as an invader and soon replaces the earlier inhabitants.

Cro-Magnon man was straight of limb with an average height of nearly six feet. His head was long, narrow and high, giving a cranial capacity in excess of that of modern man. The five male skulls found at Grimaldi average 1800 c.c., which is as much greater than the average modern brain as a small human brain is greater than that of *Pithecanthropus*.

As was mentioned, Cro-Magnon is a race of *Homo sapiens*, that is, of the same species as we ourselves. The finest physical type that the world has known, these people may have brought into Europe the bow and arrow because certainly it is not long after their appearance that these weapons are in evidence.

From the bones left in Aurignacian times, while the mammoth was still hunted, the wild horse seems to have been the favorite food. Game was plentiful in Europe at that period, and Cro-Magnon man took advantage of the comparative leisure afforded to begin the development of art—wall paintings in caves, bas relief, carved bones and ivory. There was modelling in clay also, but the statuettes are unbaked. This

ignorance of the firing of clay may account in part for the lack of pottery.

Of modern primitive peoples, the Bushmen have a culture which most nearly resembles that of Aurignacian times. The Bushmen have the bow and arrow; the men pursue large game and the women chase small game and collect vegetable food. They eat the "eggs" of termites and they eat locusts. The seeds of wild grasses are collected and stored for winter use. "How short a step it seems from this to agriculture," Sollas comments, "but to take this step requires qualities that the Bushmen never possessed and inconsistent with his unconquerable love of a wild life."

Cro-Magnon art and culture developed from the Aurignacian to the Magdalenian period in which it reached its golden age. This latter epoch coincided with a minor glaciation, Buhl, and consequently was a time of great cold. Magdalenian culture, except for its highly remarkable art, is comparable with that which the Eskimo still enjoys. The harpoon made its appearance; lamps and other implements which look typically Eskimo to us are typical too of this time.

With the final retreat of the ice at the close of the Magdalenian period (which ends, also, the Paleolithic Age) great changes occurred both in flora and fauna. The reindeer, bison and mammoth disappeared, and during this time of transition, known as the Azilian period, Cro-Magnon man, too, disappeared. According to some authorities he was absorbed or exterminated, while others believe he followed the reindeer to the north there to become merged with such groups as the Eskimo. In any case, he vanished from Europe as a race.

The remains of the Azilian period (especially those at Mas d'Azil, whence the period takes its name) show that the people of that time fed largely on shell fish and that vegetable food formed an important part of their diet; remains of acorns, haws, sloes, hazelnuts, chestnuts, cherries, plums and walnuts have been found. A handful of barley seeds was also found, but these were probably gathered wild, not cultivated. The presence of harpoons shows that they added fish to their diet, and it is likely that some flesh food was added, if only occasionally.

It is probable that the ancestors of the present races were beginning to push into Europe at this time. They seem to have come, not as a great invasion, but in small bands which penetrated farther and farther toward the Atlantic by three distinct routes.

The advent of these people ushers in the Neolithic period. They brought with them, or else developed in short order, a rudimentary knowledge of agriculture, a knowledge which grew and expanded as we know from the increasing variety of plants and from the gradual appearance of implements for preparing the soil and for harvesting crops. This new source of food supply led to the establishment of permanent camps and villages and more or less to the abandonment of the nomadic hunting life. The dog appeared about this time, first as a camp follower but soon as the constant companion of man; other domestic animals followed.

In the hearths and the kitchen middens there is no longer evidence of the splitting of the jaws of mammals and of the long and short bones of the limbs, or even of the larger foot bones, in search of marrow—a universal feature of the Paleolithic deposits.

Characteristic also of the Neolithic period is the beginning of pottery. This simultaneous introduction of pottery and agriculture has happened too many times in too many cultures to be regarded as purely accidental. These traits are so closely associated as to constitute a culture complex. Logically, a nomadic people would find pottery difficult to carry with them; only to a settled people—and in most cases that means an agricultural people—would it be of great use and convenience. Some nomadic people have pottery, to be sure, but they rarely if ever develop the making of it as an art.

An interesting speculation deals with the effect of pottery upon cooking. The crude bowls of early Neolithic times were, after all, the first water-tight vessels man had which could be subjected to heat. It may have been that cooking by boiling had its origin at this period, although some methods of boiling—that of dropping hot stones into the vessel, for example—might have been current earlier.

Neolithic man, held to a locality by agriculture, began to settle in camps and villages; unconsciously he laid the foundations for a civilization such as that even then flourishing in Mesopotamia and Egypt.

Civilization developed much faster in the valleys of the Euphrates and the Nile than it did to the North. The Egyptians, who were nicknamed "eaters of bread," cultivated cereals from early times, and cattle were kept as far back as Egyptian culture can be traced.

We have peculiar and exact knowledge of the diet of early Egyptians. According to Ruffer: "Contents of the intestines of dried pre-dynastic bodies and of mummies from dynastic to Coptic periods, prove the considerable quantity of coarse vegetable material—barley husks chiefly—that was eaten." (The pre-dynastic kings were flourishing B. C. 4500).

The Egyptians ate lentils, beans, artichokes, asparagus, beet root and cabbages. Doubtless these were cooked, but onions, cucumbers, garlic, radishes and turnips were eaten raw with bread. That diet was not wholly vegetarian, however, is shown by the pre-dynastic refuse heaps of El Toukh which have given up the bones of many animals that had served for food.

An inscription from the tomb of Belia in the XVIIIth Dynasty (1580-1350 B. C.) describes the diet of children as including bread of durra, milk ("three cows, fifty-two goats and nine she-asses") and oil. These were the children of well-to-do parents, who went to school and who carried their food with them. The children of poorer people were not so spoiled: "They give them very simple cooked foods which can be grilled before the fire, roots and roots of plants growing in marshes, sometimes raw and sometimes roasted."

The Egyptians, of course, had domestic animals—a condition which Huntington considers necessary to the development of agriculture. That this is not so is shown by the American Indians, who were many of them agricultural peoples at a time when they had no domestic animal save the dog, which certainly could not have assisted with ploughing.

It seems evident that agriculture in America had a single point of origin because maize, beans and squashes were common products wherever cultivation of the land was practiced. In many places not one food product is known to have been locally developed from an indigenous plant.

The concept of agriculture probably sprang up first in Mexico or in Central America, but the exact place and circumstances are forgotten, as also is forgotten the origin of maize. This highly interesting plant, which spread throughout both continents of the Western hemisphere, cannot survive one season without care and cultivation; someone must pick the ears of corn, remove the kernels and plant them. As far back as we know, maize had these same helpless traits. How this plant got along at all in a wild state or from what wild plant it was developed remains a mystery.

Agriculture in America had reached such a high point in prehistoric times that extensive irrigation projects were undertaken in Arizona. The ancient inhabitants of the Salado valley controlled the irrigation of at least 250,000 acres. The irrigation canals were dug by hand with wood or stone implements and the earth was borne away by means of blankets, baskets or rude litters. There is evidence that the main ditches were lined with adobe clay and fired to prevent seepage. Indeed, some of the modern irrigation systems of the region make use of the old canals dug by prehistoric Indians.

One of the most extraordinary variations of human diet is that entailed by *geophagy*—the eating of earth. This custom

is far more prevalent than one living in our culture would imagine. Earth or clay has been used, and may still be used by many peoples in times of scarcity and famine, as a food substitute to allay the pangs of hunger, giving as it does a sensation of fullness to the stomach; as a sort of condiment or relish, usually in combination with articles of food; mixed with acrid tubers or acorns as a corrective of taste; as a dainty or delicacy for its own sake; as a remedy for certain diseases; as a part of religious rites and ceremonies. Each of these uses has been known as well as morbid uses produced by or accompanying certain diseases, or due to nervous conditions.

One other dietetic variation has been widespread enough to require mention here: cannibalism. We have a single instance of cannibalism in prehistoric times. A find consisting of the charred and broken bones of fourteen individuals of the Mousterian period was uncovered at Krapina in Croatia. This is, however, the only instance of its kind in all archeology; it well may be the record of a period of famine.

It is difficult to classify the reasons ascribed to this horrible custom, so many are they and so varied. However, it seems generally that where cannibalism is practiced as a means of obtaining food and not merely as a ritual or ceremonial measure (in order, for example, to assume the characteristics or to perpetuate the spirit of the victim) the habit has its origin in a time of scarcity or famine. Apparently, once cannibalism is begun, a taste is rapidly acquired for human flesh. Sumner points out that a fork was invented in Polynesia for this kind of food long before the fork was used for any other.

This paper carefully has shunned the byways in which one might get lost in a discussion of the curious food habits of some primitive peoples, of their taboos and of the effect of these taboos on local conditions of health and sanitation. It has been our endeavor to keep to the main highway of progress.

Truly, we have come a great way since Neanderthal man crouched beside his hearth gnawing the leg of a cave bear. To him the question of diet was resolved in terms of availability. He ate what he could get. Fifty thousand eventful years, however, have brought us that degree of mastery over the resources of the earth where diet becomes a matter of choice based on knowledge rather than one of mere expediency. The chance of having been born in an inland city bars no baby from its due ration of cod liver oil. Man has become free, not only to choose those items of diet which enable him to live long and well, but even to elect the form and manner in which he will take them.

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Peake, Harold, and Fleure, H. J.: "Hunters and Artists."
Read, Carveth: "The Origin of Man and His Superstitions."
Roth, H. Ling: "The Aborigines of Tasmania."
Ruffer, Sir Marc Armand: "Studies in the Paleopathology of Egypt."
Sollas, William Johnson: "Ancient Hunters and Their Modern Representatives."
Spinden, H. J.: "The Origin and Distribution of Agriculture in America."
Sumner, William Graham: "Folkways."
Wilson, G. L.: "Agriculture of the Hidatsa Indians."

SECTION XI—*Societies, Programs and Proceedings*

AMERICAN PROCTOLOGIC SOCIETY

PRELIMINARY PROGRAM, THIRTY-FIFTH ANNUAL MEETING

CLEVELAND, MONDAY AND TUESDAY, JUNE 11-12, 1934

HEADQUARTERS: HOTEL CLEVELAND

ARRANGEMENTS: T. E. JONES, *Cleveland;* C. C. MECKLING, *Pittsburgh*

THE American Proctologic Society, organized in 1899 for the purpose of "investigating and disseminating knowledge relating to the rectum, anus and colon," is a society with a definitely limited membership, divided into Fellows, Associates, Honorary Fellows and Honorary Associates.

Regular and orthodox practitioners, members of the American Medical Association, and not affiliated with medical groups admitting those not members of the A. M. A., are hereby cordially invited to attend the 35th Annual Meeting in Cleveland, Monday and Tuesday, June 11th and 12th—the week of the A. M. A. meeting.

Physicians fulfilling the above requirements who are especially interested in Proctology are eligible to submit applications for Associate Membership after attending at least one meeting of the Society and one meeting of the American Medical Association Section.

For additional information, address the Secretary,

FRANK G. RUNYEON, M.D., F.A.C.S.
1361 Perkiomen Ave., Reading, Pa.

TENTATIVE SUMMARY OF EVENTS

MONDAY, JUNE 11th—

8:00 A.M.—Registration, Hotel Cleveland.
9:00 A.M.—First Session, Hotel Cleveland.
12:00 Noon—Luncheon at Hotel Cleveland.
1:30 P.M.—Second Session, Hotel Cleveland.
8:00 P.M.—Annual Executive Meeting (for Fellows only) in Hotel Cleveland.

TUESDAY, JUNE 12th—

9:00 A.M.—Third Session, Hotel Cleveland.
12:30 P.M.—Luncheon at Cleveland Clinic Hospital.
1:30 P.M.—Fourth Session, Clinic by Dr. T. E. Jones and Associates at Cleveland Clinic Hospital.
8:00 P.M.—Formal Annual Dinner, University Club.

Registration is necessary for admission to the above events.

THE SCIENTIFIC PROGRAM

Presidential Address—Dr. Curtis C. Meckling, Pittsburgh, Pa.
Address of Welcome—Mr. David S. Ingalls, Director of Public Welfare, Cleveland, Ohio.
Address of Welcome—Dr. C. L. Cummer, President Ohio State Medical Society.
"The Literature of 1933"—
Dr. Herbert I. Kallet, Detroit, Mich.
"Rectal Stricture—New Developments in Etiology"—
Dr. Rufus C. Alley, Lexington, Ky.
"The Frie Antigen in Benign Rectal Strictures"—
Dr. M. R. Hill, Los Angeles, Cal.
"The Relation of Anal Fistula to the Development of Cancer"—
Dr. Curtice Rosser, Dallas, Texas.
"An Atypical or Unusual Attack of Amoebiasis"—
Dr. W. T. Brockman, Greenville, S. C.
"Impalement of the Rectum"—
Dr. M. S. Kleckner, Allentown, Pa.
"Recto Sigmoid Cancer with Extensive Gangrene"—
Dr. C. E. Howard, Cincinnati, Ohio.
"Melanosis Coli"—
Dr. M. J. Synnott, Montclair, N. J.
"Avertin, With Special Reference to Its Use in Proctology"—
Dr. H. I. Silvers, Atlantic City, N. J.
"Report of Committee on Physio-therapy"—
Dr. H. I. Kallet, Chairman, Detroit, Mich.
"Report of Proctologic Society of Graduate School of University of Pennsylvania"—
Dr. H. Z. Hibshman, President, Philadelphia, Pa.
"Peri-rectal Streptococcic Cellulitix—Report of a Case"—
Dr. H. T. Hayes, Houston, Texas.
"Is Colitis a Deficiency Disease?"—
Dr. E. C. Davis, Philadelphia, Pa.
"Rationale of the Jelks Operation for Rectal Stricture"—
Dr. F. H. Murray, Chester, Pa.
Dr. H. E. Bacon, Philadelphia, Pa.
"Ligature Operation for Hemorrhoids"—
Dr. S. E. Newman, St. Louis, Mo.
"Further Observations on the Use of Hydrochloric Acid"—
Dr. G. S. Hanes, Louisville, Ky.
"Report of Cases—
"1. Amoebiasis."
"2. Primary Mucous Adeno Carcinoma of Areolar Tissue in Ischio-rectal Fossa"—
Dr. A. W. M. Marino, Brooklyn, N. Y.
"Cancer of the Rectum"—
Dr. E. P. Hayden, Boston, Mass.

CLINIC

On Tuesday afternoon Dr. T. E. Jones and associates will give an operative clinic and lectures. We hope Dr. Jones will be able to present his one stage operation for Carcinoma of the Rectum.

INFORMATION

THE ANNUAL TRANSACTIONS

The 1933 Transactions, in one volume, are now available and can be obtained from the Editor, Dr. Cecil D. Gaston, Medical Arts Building, Birmingham, Alabama. The price to non-members is Five Dollars ($5) per volume.

This volume contains all the papers and discussions presented at the 1933 Session and is full of important material. The review of Literature of 1932, by Marion Pruitt, is very valuable.

Some few copies of earlier editions are still available and are valuable to complete your record of the Society's work.

HEADQUARTERS—

The Hotel Cleveland will be official headquarters for the meeting. The registration booth will be maintained at this Hotel for Doctors and Ladies. The Scientific sessions will be held here.

Hotel reservations should be made early.

REGISTRATION FEE—

A fee of Five Dollars is in effect, as usual, for each registrant whether member, guest or member of family.

A. M. A. SECTION DINNER—

The annual dinner of the Section on Gastroenterology and Proctology will be given on Thursday evening at the Hotel Cleveland. Those desiring to attend can secure tickets from the Secretary of the Section in Cleveland.

RAILROAD RATES—

Advantage can be taken of the rates and reductions obtained by the A. M. A.

DISEASES OF METABOLISM

UNIVERSITY HOSPITAL, ANN ARBOR, MAY 14-18, 1934

Unless otherwise designated, class will meet in Medical Seminar Room, Simpson Memorial Institute

Monday, May 14

Morning

9:00-10:00 Registration. Room 2040, University Hospital.
10:00-12:00 Metabolic Mixture. Water Exchange. Inorganic Ion Exchange. Dr. Newburgh

Afternoon

2:00- 4:00 The Normal Diet. Miss MacKinnon
4:00- 5:00 Discussion.

Tuesday, May 15

Morning

9:00-10:00 Metabolism in Diabetes. Room 3410, University Hospital. Dr. Newburgh
10:00-12:00 Principles of Dietetic Treatment. Dr. Newburgh

Afternoon

2:00- 4:00 Calculation of Diets. Miss MacKinnon
4:00- 5:00 Discussion.

Wednesday, May 16

Morning

9:00-12:00 Diabetic Clinic. Room G 106, University Hospital. Dr. Newburgh, Miss MacKinnon

Afternoon

1:00- 2:00 Teaching of Patients. Room G 106, University Hospital. Miss MacKinnon
2:00- 4:00 Preparation of Diabetic Diets. Room B 114, University Hospital. Miss Cartmill

Thursday, May 17

Morning

9:00-10:00 Correlation of Various Classifications of Renal Disease. Dr. Lashmet
10:00-11:00 Normal Physiology and Abnormal Variations of Kidney Function. Dr. Lashmet
11:00-12:00 Nature of Edema. Dr. Lashmet

Afternoon

2:00- 4:00 Functional Tests in Renal Disease. Dr. Lashmet

4:00- 5:00 Treatment of Renal Disease. Dr. Lashmet

Friday, May 18

Morning

9:00-12:00 Calcium Metabolism. Normal and Abnormal. Room 3410, University Hospital. Dr. Freyberg

Afternoon

2:00- 4:00 Preparation of Nephritic Diet. Miss Enke
4:00- 5:00 Discussion.

TEACHING STAFF

L. H. Newburgh, M.D., Professor of Clinical Investigation in Internal Medicine.
F. H. Lashmet, M.D., Assistant Professor of Internal Medicine.
R. H. Freyberg, M.D., Instructor in Internal Medicine.
Genevieve Cartmill, B.E., Instructor in Dietetics, Department of Internal Medicine; Dietitian, Metabolism Service.
Frances MacKinnon, A.B., Dietitian, Diet Therapy Clinic.
Gladys Enke, B. S., Dietitian, Ward Service.

PRACTITIONERS' COURSE

RECEIVING AND HERMAN KIEFER HOSPITALS, DETROIT, MICHIGAN, JUNE 18-22, 1934

Monday, June 18

Morning

8:00 Registration. Receiving Hospital
8:30 Symposium on Gastro-Intestinal Disease.
Peptic Ulcer.
a. Differential Diagnosis from Clinical Standpoint.
b. Differential Diagnosis from X-ray and other Laboratory Standpoints.
Dr. Hugo A. Freund, Dr. Wm. A. Evans
10:00 c. Medical Treatment. Dr. C. E. Vreeland
11:00 Gastro-intestinal Neuroses. Dr. H. A. Reye

Afternoon

1:30 Complications of Peptic Ulcer and Indication for Surgical Treatment. Dr. F. G. Buesser
2:30 Amebic Dysentery and Ulcerative Colitis. Diagnosis and Treatment. Dr. B. C. Lockwood
4:00 Gross specimens. Gastro-intestinal Disease. Dr. O. A. Brinse

Tuesday, June 19

Morning

8:00 Gall Bladder Disease. Clinical Picture. Differential Diagnosis. When to Operate. Dr. R. J. Schneck
9:00 Agranulocytosis. Dr. Hugo A. Freund
10:00 Ano-rectal Disease. Methods of Examination. Office Procedures. Clinic. Dr. L. J. Hirschmau

Afternoon

1:30 Symposium on Heart Disease. Classification, History Taking, Signs and Symptoms of Heart Failure. Dr. Norman E. Clarke
2:30 Pathologic Physiology. Dr. Douglas Donald
3:30 X-ray and Electrocardiography in Heart Disease. Dr. Douglas Donald, Dr. J. C. Kenning

Wednesday, June 20

Morning

8:00 Diabetes mellitus. Requirements for Diagnosis. The Pre-Diabetic State. Dr. Richard McKean
9:00 Principles of Treatment. Dr. Richard McKean
10:00 Laboratory Procedures. Preparation of Diets. Dr. Daniel P. Foster

Afternoon

1:30 Factors in Estimation of Surgical Risk. Dr. E. D. Spalding
2:30 Pre-operative and Post-operative Care. Dr. L. J. Morand
3:30 Injuries to the Eye. Dr. Don M. Campbell

AMEBIASIS EXHIBIT AT THE CLEVELAND SESSION OF THE AMERICAN MEDICAL ASSOCIATION, JUNE 11-15, 1934

An extraordinary opportunity will be presented at the Cleveland Session of the American Medical Association, June 11-15, for the study of amebiasis. A scientific exhibit covering all phases of the subject will occupy a large space on the main floor of the Public Hall which will house all sessions of the meeting. As the list below indicates, some of the best known authorities in this field will be in attendance.

The microscopic diagnosis by special staining methods on stool smears will be demonstrated by Dr. Wm. M. James of Panama, who has been a student of amebiasis ever since the building of the Canal. Sixty microscopes will be set up aside from the general exhibit so that those interested can take time to study good specimens. Microscopic and gross pathology will also be demonstrated.

Living cultures of amebae will also be on exhibit, prepared by Doctor Francis Bayless of Western Reserve Medical School, following the method of Doctor Cleveland of the Harvard School of Tropical Medicine.

The epidemiological and public health aspects of the disease, especially the data obtained from the Chicago epidemic will be presented by the Chicago Health Department. The therapeutic aspects of the disease will also be presented by charts and by actual samples of the various drugs used.

In connection with the scientific exhibit there will also be *an entire afternoon*—Tuesday, June 12th—devoted to the subject of amebiasis in the Clinical Lectures in the Section on General Medicine.

The presentation of the subject is so comprehensive as to merit the attention of all students of gastro-enterology.

The approved list of exhibitors is as follows:

C. D. Leake, A. C. Reed, H. H. Anderson, H. G. Johnstone, Hooper Foundation, San Francisco.

W. M. James, Lewis R. Bates and Lawrence Getz, Panama.
Diagnosis and Pathology of Amebiasis.
(Gross and microscopic pathology. About 60 microscopes showing stool and culture preparations of amebae).

Manfred Kraemer and Maurice Asher, Newark, N. J.
Procto-Sigmoidoscopic Method for the Diagnosis of Amebiasis.

Francis Bayless, Western Reserve Medical School, Cleveland.
Living Cultures of Amebae.

Isaac D. Rawlings, Chicago, Health Department, Chicago.
The Chicago Outbreak together with pathologic specimens and cultures of amebae.

Army Medical Museum, Washington, D. C.
Enlarged photomicrographs showing entameba histolitica compared with other amebae and various pathologic and histologic sections of lesions.

V. C. Rowland, Cleveland,
Chairman Scientific Exhibit.

AMERICAN JOURNAL OF

DIGESTIVE DISEASES AND NUTRITION

CONTENTS

SECTION I—CLINICAL MEDICINE — Page

THE RESULTS OF TREATMENT—MEDICAL AND SURGICAL—IN GALL BLADDER DISEASE—FROM A CLINICIANS' VIEWPOINT—*Thomas R. Brown, M.D.* — 221

LATE MANIFESTATIONS OF AMEBIASIS—*R. W. Mendelson, M.D.* — 228

COMPLEMENT FIXATION TEST FOR AMEBIASIS (PRELIMINARY REPORT)—*Emil Weiss, M.D. and Lloyd Arnold, M.D.* — 231

LAMBLIASIS SIMULATING CHOLELITHIASIS—REPORT OF TWO INSTANCES—*Meyer Golob, M.D.* — 233

BRILLIANT BLUE F.C.F., A NEW DYE FOR DIAGNOSTIC GASTRO-INTESTINAL STUDIES—*Arthur C. Taylor, M.D.* — 239

THE OCCURRENCE OF A PERNICIOUS ANEMIA SYNDROME IN THE PRESENCE OF NORMAL GASTRIC ACIDITY—REPORT OF AN INSTANCE—*A. L. Levin, M.D.* — 240

ABSTRACTS — 242

SECTION II—EXPERIMENTAL PHYSIOLOGY

THE INFLUENCE OF THE PYLORUS UPON THE REGULATION OF THE ACIDITY OF THE GASTRIC SECRETION—*William Walsh Lermann, M.D. and Lyle M. Nelson, Jr., M.D.* — 245

ABSTRACTS — 248

SECTION III—NUTRITION

A STUDY OF OBESITY IN AN OUTPATIENT CLINIC—*Edgar C. Beck, M.D. and Roger S. Hubbard, Ph.D.* — 250

THE INCIDENCE AND SIGNIFICANCE OF DISEASE OF THE GALL BLADDER AND LIVER IN PERNICIOUS ANEMIA—*Frank H. Bethell, M.D. and Bernard D. Harrington, M.D.* — 256

ABSTRACTS — 259

SECTION IV—ROENTGENOLOGY

FACTORS OF ERROR IN ROENTGENOLOGIC DISTINCTION BETWEEN THE NORMAL AND THE DISEASED STOMACH AND DUODENUM—*B. R. Kirklin, M.D.* — 260

SECTION V—THERAPEUTICS

SECTION VI—ABDOMINAL SURGERY

CONSERVATIVE SURGICAL TREATMENT OF ULCER OF THE STOMACH AND DUODENUM—*E. Starr Judd, M.D. and George W. Waldron, M.D.* — 262

AN ANALYSIS OF THE RESULTS OF BILIARY TRACT SURGERY—*John Tilden Howard, M.D.* — 270

ABSTRACTS — 271

SECTION VII—SURGERY OF THE LOWER COLON AND THE RECTUM

SECTION VIII—EDITORIAL

THE PROMPT DISSEMINATION OF MEDICAL KNOWLEDGE — 274

MEDICINE: A PROFESSION, TRADE OR TENT SHOW? "DIET DERBY" — 275

TO THE FAD-BOUND OVERWEIGHT (*Poem*) — 275

CLEVELAND CLINIC MEMBERS PLACED ON EDITORIAL COUNCIL — 276

SECTION IX—BOOK REVIEWS

NUTRITION, *Graham Lusk, Sc. D., M.D., LL.D.* — 277

THE VITAMINS IN HEALTH AND DISEASE—*Barnett Sure, Ph.D.* — 279

SECTION X—AFTER "HOURS"

THE GOLD-HEADED CANE — 280

SECTION XI—SOCIETIES, PROGRAMS AND PROCEEDINGS

A SURVEY OF ENZYME TESTS — 286

PUBLISHED MONTHLY BY THE SANDFIELD PUBLISHING CO., FORT WAYNE, INDIANA

VOLUME I — JUNE, 1934 — NUMBER 4

The Discoverer of Insulin Honored by King George V.



Sir Frederick Banting, K. C. B. E.

The list of the King's birthday honors (June 3) included the name of Dr. Frederick G. Banting, discoverer of insulin, and member of the Editorial Council of the American Journal of Digestive Diseases and Nutrition.

Dr. Banting was made a Knight Commander in the Civil Division of the Order of the British Empire, and will now be known as Sir Frederick Banting, K.C.B.E. This honor, given because of his discovery of insulin in 1921, was delayed probably because the Canadian Government ruled against titles for resident Canadians for a number of years, a ruling recently removed.

To the profession at large, as well as to the general public, this honor will be regarded as a well deserved one. If any deed in civil life merits the highest honor which a sovereign may confer upon a subject, the discovery of insulin is an outstanding example.

Dr. Banting's unusual modesty has become almost proverbial during the last twelve years, while many honors were being heaped upon him. His generosity of mind and character have been felt by all who have come in contact with him. He possesses decidedly the research type of mind and has the faculty of quickly distinguishing between the important and non-essential in any given question. He is now in charge of the Banting Institute at Toronto where a large number of interesting research problems are being investigated by many workers. The correlation of these various investigations requires considerable attention, but Dr. Banting persists in working personally on individual problems of his own. In addition to modesty and generosity of spirit, he possesses an indomitable will, a tireless energy of mind and body and also a personal simplicity which makes him always "just one of the boys."

His hobby is painting and he is seen to best advantage within the precincts of his studio surrounded by easels, paint brushes, and tubes of pigment. His work in oils possesses real merit and many of his landscapes have been exhibited in Toronto and elsewhere. During an Arctic cruise six years ago, many of his most striking landscapes were made from the deck of a Canadian Government Steamer, and they reflect the austere coloring of icebergs and snow and open stretches of green water.

This Journal has been gratified to be able to consult Dr. Banting as one of its scientific members and we desire now to congratulate openly the discoverer of insulin on his recent splendid distinction.

Editors and Council.

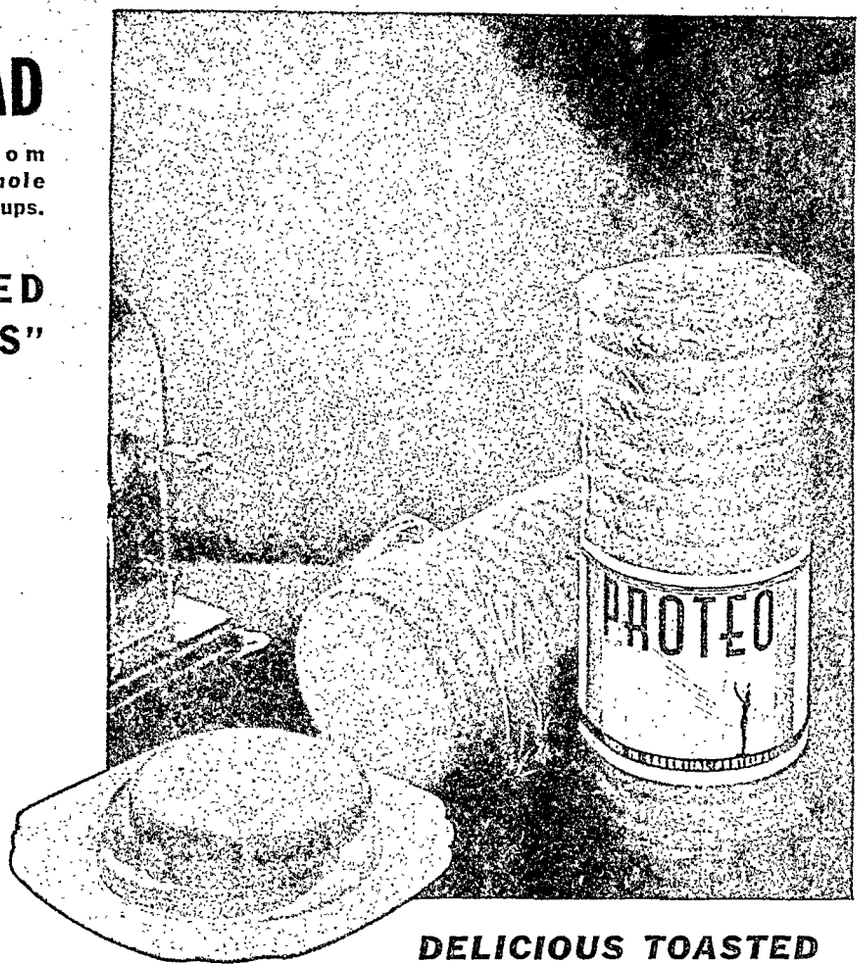
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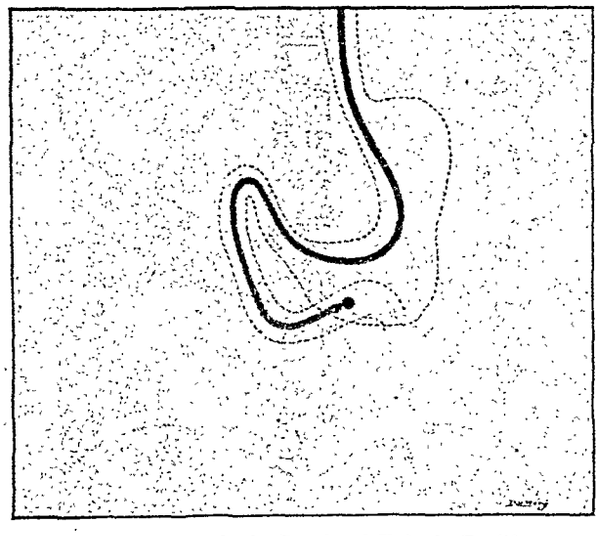
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ALLERGY

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SECTION I—*Clinical Medicine: Diseases of Digestion*

THE RESULTS OF TREATMENT—MEDICAL AND SURGICAL—IN GALL BLADDER DISEASE

FROM A CLINICIAN'S VIEWPOINT *

By

THOMAS R. BROWN, M.D.†

BALTIMORE, MD.

IT HAS seemed to me that it may be of interest for a medical clinician carefully to analyze the results of treatment in biliary tract disease, be that treatment medical, surgical or a combination of both; most of the previous analyses have been made by our surgical brethren. It would seem helpful to determine from the point of view of the clinician, who sees these patients over a long period of time, the number that has really been cured or materially helped and the number in whom discomfort, pain, indigestion or other symptoms remain, and then to compare our figures with those of the surgeons.

For this purpose, my associate, Dr. Howard, carefully has analyzed all of our cases whose after-histories thoroughly could be investigated, not by a postal card survey, but by intelligent re-study of their cases: he will present the complete analyses of these cases in another contribution published in this number of the *Journal*.

No one can gainsay that as regards the *diagnosis* of gall bladder disease we have made tremendous advances in the past few years:—the X-ray studies by the Graham method, analyses of the duodenal contents in certain cases, ever increasing knowledge of the clinical pictures of gall bladder and biliary tract disease, a knowledge which has been brought about, primarily, by ever closer co-operative efforts between surgeon and clinician in the study of these affections.

But notwithstanding all these advances, still there is a considerable diversity of opinion as to the correct appreciation of symptoms and signs, and of management in many of these patients: chronically diseased gall bladder with gastric dyspepsia, gall bladder with symptoms referred elsewhere, those with attacks of biliary colic at long intervals, etc., although, of course, it is quite obvious that in certain conditions, (as for example, repeated and severe attacks of gall bladder colic, empyema of the gall bladder, fulminating cholecystitis), one, and only one method of attack is justified, and that is the surgical.

It is a consideration of these principles as to etiology, diagnosis and therapy based on the newer knowledge, and with a rather extensive personal experience in this field, which is the reason for this paper. How shall one answer the questions:

I—HAS THE PATIENT GALL BLADDER TROUBLE, AND IF SO, WHAT IS ITS NATURE AND SEVERITY?

II—WITH GALL BLADDER DISEASE CERTAIN OR PROBABLE, WHAT IS THE PROPER TREATMENT?

*From the Division of Digestive Diseases, The Johns Hopkins Hospital, Baltimore, Maryland.

†Associate Professor of Medicine, Johns Hopkins University; Chief of the Division of Digestive Diseases.

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I. DIAGNOSIS AND APPRAISAL OF NATURE AND SEVERITY

In the first place, we must entirely change our attitude toward the gall bladder. We cannot regard it as a definite entity such as the heart or the kidney or the eye. It must be considered as part of a system—liver, extra-hepatic and intra-hepatic biliary ducts, gall bladder itself—because, when gall bladder disease is present, usually there is a greater or lesser concomitant and associated pathology in the rest of this system. Thus, the result of our therapy, notably our surgical therapy, will be dependent largely upon whether this associated involvement of liver and biliary system is great or small; whether the major portion of the pathology will have been removed by the attack on the gall bladder; whether the compensatory dilatation of the biliary ducts and radicles, following cholecystectomy, will take care of the associated hepatitis or cholangeitis or whether, in reality, it is liver and biliary tract which play the larger *role* in the syndrome presented and that represent the primary trouble, and whether the gall bladder is playing only a minor and secondary *role*.

For this viewpoint, this consideration of liver and entire biliary system rather than of the gall bladder alone, we have sound *embryological, anatomical and physiological*, as well as clinical, justification.

The liver and gall bladder are developed together from the first evagination or bud which springs from the gut, the solid, cephalic portion of this bud giving rise to the liver, the hollow caudal part, continuous with the lumen of the gut giving rise to the extra-hepatic ducts, with the distal portion enlarging to form the gall bladder. Thence, the *embryological* evidence of their homogeneity.

The gall bladder, although in the main covered by peritoneum, is connected with the liver in a portion of its superior surface by areolar tissue containing lymphatics and blood vessels through which, obviously, infection may flow in either direction. This, with similarity in blood and nerve supply, the *anatomical* basis. Occasionally, of course, the gall bladder is entirely covered by peritoneum, is not directly connected with the liver, but is dependent from it by pure peritoneal attachment which may very occasionally become elongated to such extent that the gall bladder may be situated in the lower right quadrant of the abdomen and produce a tumor then very difficult or impossible to diagnose. We saw such an anomaly last year, which anomaly, incidentally, only was correctly diagnosed at operation. The proximity of the gall bladder to liver, to transverse colon, duodenum and pylorus, is the obvious cause of the confusing symptoms so often presented, especially as it may vary somewhat in position; may even be to the left of the median line and may show

certain anatomical abnormalities such as congenital communication between hepatic and cystic ducts or separate openings of hepatic and common ducts into the duodenum, and extremely rarely there may be a double gall bladder. Another factor of extreme interest in the consideration of the association of diseases and the confusing over-lapping of symptoms in biliary tract disease, is the position of biliary and pancreatic ducts, incidentally very closely connected anatomically in their fusion in the duodenal wall — in about 96% just proximal to the papilla of Vater, though in about 4% of the cases fusion is seven centimeters higher; this occurrence, by some, has been supposed to be the cause of pancreatic lesions, notably acute pancreatitis secondary to gall bladder disease.

Physiologically, of course, liver, biliary tract and gall bladder must be considered together. It will take us too far afield to go into the complex subject of liver physiology, but in one of its many functions, the formation of bile, the role of the gall bladder is now fairly well understood. The work of Rous, on dogs, has shown that its major function, at least, is the concentration of the bile; the fact that this investigator showed a variation in concentration-power, *in normal animals*, from three to eleven times (possibly partly based upon anatomical variations) must make one a bit skeptical as to the diagnostic value of faint gall bladder shadows, after dye administration, as indicating evidence of pathology. May not some of these Roentgen-ray observations represent simply variations in concentrating power?

As to the *motor mechanism* of the gall bladder, there is much difference of opinion. Although many do not recognize it, the weight of evidence seems to be in favor of a true sphincter, the sphincter of Oddi. On the other hand, the weight of evidence seems to be *against* the view that muscular contractions of the gall bladder wall play a significant role in its emptying. The absence of such a mechanism recently has been shown very beautifully by Marrazzi, who studied the gall bladder by direct observation through an endoscope and who showed definitely that neither under ordinary physiological influences nor after the use of drugs which have a definite effect on smooth muscle elsewhere, nor by mechanical or electrical stimulation could such contraction be denomstrated.

As to the *role* played by the gall bladder in the *formation of cholesterin*, here again we meet widely divergent views. The evidence, however, seems to be most in favor of the view that the gall bladder absorbs cholesterin, an opinion supported by Aschoff, rather than that there is any secretion of cholesterin by the wall itself. In fact, there is increasing evidence that the intake of lipoids by mouth plays little or no role in cholesterin metabolism. There is, therefore, slender evidence in favor of excluding oils, eggs, cream and other fats from the diet of those with cholelithiasis except, obviously, in cases which are associated with jaundice when, of course, reason for such exclusion from the diet is the well known deficient digestion of fats in the absence or limited presence of bile in the intestine.

Etiology—In regard to the etiology of biliary tract disease, something is known: a great deal is still unknown. There seems to be evidence that overeating, a sedentary life, lack of exercise and the incidence of obesity all, in a way, predispose to it. There is a fairly general belief that pregnancy and the puerperium play a *role;* that many patients date their first definite symptoms—severe pain, jaundice, upper right quadrant discomfort—from the last days of pregnancy and the first days of the puerperium; the attacks often are forgotten in the lapse of time and are only elicited by the careful history which is so essential in the unraveling of all abdominal cases.

On the other hand, some observers are quite convinced that gall bladder pathology is relatively not more frequent in women who have borne children than it is in those who have not, although, personally, I can hardly escape from the conviction that, in some cases, there is a definite connection, possibly due to inactivity, to pressure, to disturbed blood chemistry or possibly to infection.

Preceding infections, notably *typhoid fever*, unquestionably have an influence in some cases. The typhoid bacilli presumably pass from the intestine by way of the mesenteric glands, lymphatics and thoracic duct into the general circulation; in their excretion by the bile they may be so concentrated in the gall bladder as to produce temporary or permanent pathology, cholecystitis or cholelithiasis. This, however, occurs far less frequently than formerly was supposed. In our experience not more than 5% of the cases of cholelithiasis seems to be of this origin, but, in certain of these cases, living typhoid bacilli still may be obtained in the bile and from the center of stones, although the infection may have occurred many years previously. It is this type of case, as well as the so much commoner, similar, urinary tract typhoid infections, which is such a menace as a carrier. Other infections, notably influenza, may act similarly, although the path of infection may be somewhat different.

Cardiac disease unquestionably predisposes to cholelithiasis, probably due to the inevitable inactivity of the patient, the passive congestion of the liver, the disturbance of digestive function with its frequent absence of gastric acid and the corresponding increase in the gastric and duodenal bacterial flora. Thus, in the Royal Infirmary at Manchester, gallstones were present in 10.4% of 504 patients with cardiac pathology and in only 5.1% of cases with no such pathology. On the other hand, the reverse equally is true that definite myocardial changes may be referable to biliary tract disease with its pain, its fever, its jaundice, its excess in the blood of bile salts, pigments and possibly other toxins.

Cholesterin stones, the so-called metabolic stones, possibly may be due to excessive cholesterin in the blood, but it is far more likely that they are due to certain changes in the bile by the lessening of the solubility of this substance or lowering the absorptive power of the gall bladder wall.

There are many *precancerous lesions* in the digestive tract—leukoplakia, peptic ulcer, intestinal polyps—but none more interesting than the *role* of cholelithiasis in the origin of gall bladder cancer: 70% of those dying with this disease have gallstones as well.

Cirrhosis of the liver certainly predisposes to biliary tract and gall bladder disease; probably by direct infection, possibly by disturbances in bile formation; the significance of the liver in cholelithiasis is well shown by the not infrequent association of hepatic and gall bladder lithiasis and the development of stones in the hepatic biliary system *after* cholecystectomy.

On the other hand, the vast majority of diseases of the biliary tract cannot be explained by any of these factors. It would seem that they must have their origin in infection from the gastro-intestinal tract, but whether the lower portion of this tract, the colon, the appendix, the terminal ileum, or the duodenum exerts the larger primary influence, still is a moot question.

In regard to the duodenum, it is worth remembering that, while under normal conditions the stomach and the duodenum practically are sterile, any condition which leads to gastric or duodenal inflammation, especially, (as is the case of most patients) with a temporary or permanent absence or diminution of hydrochloric acid in the gastric contents, the duodenum is filled with all forms of intestinal microorganisms, notably the colon bacilli, although streptococci also are met with as they are markedly prevalent in the ileum under normal conditions and in smaller proportion in the colon. It is highly probable that this group of organisms is, in the majority of instances, the cause of infection of gall bladder, liver and biliary tract, with complicating acute or chronic cholecystitis, empyema, gangrene or suppuration. It is amazing how rapidly colon bacilli may appear in the

duodenum in such conditions, as for instance following an acute gastritis, a condition which usually is associated with a temporary achlorhydria.

The path of infection of this organism (colon bacillus) from intestinal tract to biliary system is still undemonstrated. Certainly it is not proven that its path is similar to that of the typhoid bacillus, *i. e.*, through mesenteric glands, lymphatics, thoracic duct and general circulation. It is possible that its path is the portal system but there is very little experimental evidence to prove this opinion. It might be through the lymphatics directly to the liver, producing first a liver infection and, thence, by the lymphatic system between liver and gall bladder, into the gall bladder as a secondary infection, as Graham and many others believe; many others think the reverse is more probable, that is, the gall bladder is primarily, the liver secondarily, infected. *B. coli* may represent an ascending or retrograde infection from the diseased duodenum; this view is held by a number of investigators. lesion, The in such circumstances, first is superficial and relatively easy to cure: later there occurs invasion of the gall bladder wall. Obviously such lesion is much more resistant to treatment.

The frequent *association of duodenitis and gastric disturbances* with gall bladder pathology, speaks in favor of the latter of these views, while perhaps the even more frequent association of gall bladder disease and appendicitis is more in favor of a direct lymphatic infection from the lower intestine. There is considerable experimental evidence to support this opinion but perhaps not more experimental evidence than is in favor of other views.

Some observers still believe with Rosenow that many cases of biliary tract disease are due to *special strains of streptococci* which originate in periapical abscesses, diseased tonsils or nasal accessory sinuses and pass directly through the blood stream, that is, by way of the cystic artery. While it is possible that such foci of infection may play a part in some of the severer cases when virulent streptococci are found in the throat and also in the gall bladder, it is highly improbable that they exert a large influence in chronic infections. Many observers have not been able to confirm Rosenow's work; according to some of these investigators not more than 7% of the organisms found in diseased gall bladders are streptococci, the vast majority being colon bacilli.

Finally, one must not forget the possibility that *anatomic abnormalities*—kinking of the ducts, abnormal position of the gall bladder and a physiologic variation in the concentrating power of this viscus—may be contributory etiologic factors.

Symptomatology. The symptoms in gall bladder disease may be definite, localized and crystal-clear or they may be diffuse, referred elsewhere, blurred and indefinite. No cases are easier to diagnose than the former, none more difficult than are the latter.

Nothing could be clearer cut than the typical gallstone colic, with or without jaundice, the localized, agonizing pain requiring morphine, the tenderness, the nausea, the epigastric distention, often a white stool and dark urine give a picture almost impossible to mistake. Yet we have all had patients in whom, with such histories, gallstones have not been found, but we have noted either cholecystitis alone (in this event it is admitted that there may have been a single stone which had been passed) or no evident gall tract disease but instead, renal calculus, pyelitis, spastic colon with mucous colitis, diseased appendix, duodenal ulcer, evidence of upper right quadrant adhesions or absolutely no abdominal pathology. In the last circumstance, the symptoms presumably were due to coronary disease, non-demonstrable arthritis of the spine, localized neuritis, a gastric crisis of locomotor ataxia or simply a localized manifestation of hysteria or psychoneurosis.

Again, it is hard to mistake an acute cholecystitis with its local tenderness—often exquisite—its fever, its nausea, possibly its slight jaundice, its leucocytosis and often the palpable gall bladder tumor. Yet again, it is extremely difficult to eliminate certain rare, other possibilities and, in certain instances to differentiate a mild infection, which will clear up spontaneously, from a severe suppurative or gangrenous process. In the latter lesion, and in most cases, the infection will be kept from becoming a general peritonitis by the enfolding arms of the ever-protective omentum, one of whose main functions is the localizing of infection. Yet, in certain cases, this mechanism may not be effective and immediate surgery to save life may be necessary. It is for this reason that an ever-increasing number of surgeons believe that the "acute gall bladder" should be treated exactly as is the "acute appendix," namely, by immediate surgery. Many still believe that, in the vast majority of cases, it is wiser to wait for the infection to subside with subsequent performance of an interval operation if necessary. Unquestionably, in many cases, the severity of the infection can be determined by careful clinical observation, the study of temperature curves, the frequent estimation of *total* and *differential* leucocyte counts, the presence or absence of sweats, the variations in the pulse, the general condition of the patients, the evidences of toxemia. However, there certainly are some patients in whom suppuration or gangrene may develop with no local, general or laboratory findings which, ordinarily, would arouse any suspicion as to their possibility.

In his recent very careful review of all the gall bladder operations in the San Francisco Hospital from 1919 to 1931 Mentzer is convinced that . . . "advanced, acute cholecystitis cannot be recognized in many instances even by the ablest physicians; that what appears to be a mild or moderately severe cholecystitic inflammation clinically, may actually be fulminant and that perforation and gangrene of the gall bladder occur more frequently than is usually supposed."

Recently, I have seen several such cases and personally believe that for some reason there has been a definite increase of these fulminating cases in the past few years. In two of my cases the acute lesion seemed to follow immediately after an attack of grippe with bronchial pneumonia, but whether this was the real cause one cannot say.

Thus, while in gallstone colic and in many cases of infected gall bladders, the symptoms are fairly definite and the diagnosis easy, nothing is *more* difficult than is the diagnosis of disease of the biliary tract in that large group of chronic, and small group of acute, cases, where there are few or indefinite local symptoms, and almost entirely the symptoms are referred elsewhere. The reason for this referring or overlapping of symptoms easily is understood when one recalls the close juxtaposition of liver and gall bladder, heart, lungs, stomach, duodenum and transverse colon, when we remember the great similarity in blood and nerve supply of this viscera and realize with Charles Mayo . . . "How diverse may be the paths through which painful sensations may leave the abdomen." (Many, however, still believe it is a viscero-sensory reflex and not the presence of true nerve fibres which explains such phenomena.)

A pain in the right shoulder or a persistent backache, usually in the right side, may be the only evidence of biliary tract disease—the former probably due to the fact that a branch of the phrenic nerve unites with the sympathetic fibres of the celiac plexus to form the phrenic plexus. The picture absolutely may simulate duodenal ulcer—hunger pain, periodicity, persistent defect in the X-ray plate, even extensive hemorrhage—and yet a *normal* duodenum but a *diseased* gall bladder is found at operation: the reverse is also true: that is, an ulcer in the second portion of the duodenum may present only a clinically typical gall bladder syndrome. In trying to determine the cause of extensive hemorrhage, one should never forget the possible *role* which an unsuspected gall bladder may play, probably due to an associated marked engorgement of the veins in the stomach or the duodenum. Similarly, it is wise to remember that even a diseased appendix also may be associated with severe hemorrhage. It is, however, well to recollect that the simul-

taneous presence of peptic ulcer or appendicitis and gall bladder disease is not uncommon.

A diseased gall bladder with its achlorhydria, the anorexia and loss of weight, met with not infrequently, accompanied by a persistent X-ray filling defect in the stomach, often due to adhesions between gall bladder and pylorus, may so completely simulate gastric carcinoma that only at operation the mistake is discovered.

In a few, fortunately a very few, cases the symptoms may be entirely cardiac—usually simulating coronary disease, occasionally myocardial weakness—but where there is present no actual heart disease, then the cardiac group of symptoms reflexly is produced from a diseased gall bladder. Recently, we have reported a series of such cases where all the cardiac symptoms disappeared after cholecystectomy. However, one must never forget that the reverse of the picture—that is, coronary disease with exclusively abdominal symptoms usually suggesting gallstone colic—is far more common. Therefore, clinicians must be very sure and very careful before they diagnose cardiac syndromata as biliary in origin and advise cholecystectomy as treatment.

We have discussed, purposely, the *uncommon* referred symptoms of gall bladder disease. Much more commonly, of course, the symptoms are referred to the stomach. Certainly it is true that a large number of the flatulent dyspepsias met with, mostly in women, but occasionally in men of middle life (discomfort and distention after meals, marked discomfort during the night, fulness, eructations, palpitation and sometimes slight nausea), are dependent upon unrecognized gall bladder disease, with or without stones. Sometimes the discomfort radiates to the gall bladder region, there is local upper right quadrant tenderness on deep pressure, but often there is no suggestion of any gall bladder pathology: the gastric syndrome may be the only evidence of cholelithiasis or cholecystitis. Sometimes, on close questioning, the history of a former acute attack may be elicited; more often, there has been no definite biliary tract history. The syndrome is sufficiently common to be dignified by the name "biliary dyspepsia;" certainly, the gall bladder should always be suspected as a potential cause of atonic flatulent dyspepsia, especially if the symptoms are much more marked during the night.

In certain cases of *diabetes* gall bladder pathology is found without antecedent dyspeptic history and in certain cases there is definite history of previous attacks. Unquestionably it is true that biliary tract pathology, recognized or unrecognized, is present in a certain percentage of diabetic patients, varying from the 1% of Naunyn to the 41% of Eustis.

Sometimes slight, persistent or periodic *fever* may be the only sign of the gall bladder lesion. There still is a considerable group of physicians, notably Wilkie, which believes that a diseased gall bladder is a very potential factor as a focus of infection in the etiology of various widely different ailments, *e. g.*, arthritis, nephritis, myocarditis and other chronic inflammatory processes.

Personally, I have seen very few patients in whom such an etiologic relationship definitely could be proved. Many times, I have been extremely disappointed by failing to note any benefit in this group of cases after cholecystectomy and I have become extremely skeptical as to the advisability of gall bladder removal as proper treatment for such patients. Hardly do I remember a case which has been materially helped thereby. On the other hand, it is perfectly true that fever, toxemia or jaundice of a long lasting biliary tract infection possibly may be the source of trouble elsewhere; it seems quite definitely proved that myocardial disease can be produced by this mechanism.

It is a disturbing organ, this gall bladder, with its localized symptoms in one case, its referred symptoms in another, its mimicry of disease elsewhere and its ability to mirror disease in other organs. To make the maximum number of correct diagnoses and to minimize failures, all the possibilities, which we have briefly sketched above, carefully must be considered and weighed, for it is only by the unhurried estimation of systematically and accurately gathered facts combined with the proper examinations and appropriate laboratory studies, that we may hope to reach a correct appraisal of the condition present in each individual.

Diagnosis. How then may we best arrive at a correct or at least a probable diagnosis? In my experience the very best information comes from an old-fashioned procedure, far too often forgotten in the passion for short-cuts to knowledge by laboratory or objective methods: (1) *The history of the case!* I have found that, notwithstanding the notable advances made in X-ray diagnosis, in the study of duodenal contents and in other technical methods which are always increasing our already very large debt to the roentgenologist, the research worker and the technician, it is from a carefully taken, thorough and well-digested history of the case—the noting of the mode of onset, the early symptoms, the change of symptoms, the picture as it progresses and the various factors which modify it—it is from such that we can obtain the most reliable diagnostic data.

The history, sometimes almost forgotten, of a severe attack or attacks of right epigastric or hypochondrium pain which requires morphia hypodermatically for its relief, the story of attacks with jaundice and slight rise in temperature, of acholic stool and cholic urine, or persistent or remittent pain or tenderness in the upper right quadrant or of nocturnal flatulent gastric dyspepsia,—it is from these departures from the normal that often we make our final diagnosis and plan our treatment. However, never should one forget, in the wise words of Professor Haldane, that in studying biological phenomena . . . "we must always keep the whole organism in view." It is of singular importance in this field where the symptoms so often are difficult to interpret.

Two years ago, in a careful analysis of the large amount of material in our Clinic, we found that by such a method alone, that is, careful *analysis* of the history, not only *digestive history* but the *entire history* of the patient with the usual routine physical examination, slightly less than 85% correct diagnoses were made in cases of biliary tract disease as judged by the subsequent history of the cases—usually surgical.

(2) Next in value, of course, is *cholecystography* by the Graham method. But our experience has been that by this method alone the chance of error is somewhat greater than by analysis of the history of each patient alone, if judged by the same criteria. In our series by the Graham method, we have found both a positive and negative error of about 20%; in other words, about 20% of the cases diagnosed roentgenologically as *pathological* were found to be *normal* and about 20% of those diagnosed as *normal* were found to be *pathological*. However, we have used practically exclusively the oral technique and the margin of error is certainly somewhat greater by this method than it is after the intravenous administration of the dye. It is needless to say that, in all suspected cases, one should never be satisfied with but one series of films. But, as we have already mentioned, variation in the concentrating power of the gall bladder and of the absorptive power of the intestinal mucosa and probably anatomical variations in the normal gall bladder as well, must *per se* produce variations in density of shadow which are likely to be regarded as pathological, but which in reality may be within normal limits.

In the case of the diagnosis of gallstones by cholecystography, we believe that the possibility of error is very much greater, some clinicians claiming that as many as 50% of subsequently demonstrable gallstones have not been visualized in the X-ray pictures.

(3) As to the value of the so-called *medical drainage of the gall bladder* (method of Lyon) as a diagnostic procedure, there is the widest divergence of opinion. Some physicians place the utmost confidence in it, others deny its value altogether. Personally, I do not use it as a routine measure, mainly because with the tendency to subacidity and achlorhydria so common in biliary tract disease, the normal, sterile duodenum

teems with all kinds of bacteria and therefore bacteriological studies seem to me of little or no value with the exception of those relatively rare instances where unusual micro-organisms or some form of protozoan, such as *Lamblia*, are found in large numbers. The presence of a few pus cells cannot be of much significance because of their possible origin from pharynx, stomach or duodenum, while, in our experience at least, the presence of cholesterin or bilirubin calcium crystals is not diagnostic of gallstones—such are frequently found when no such pathology is present.

On the other hand, I have found biliary tract syphonage of great value in certain cases, mostly those of extensive hepatitis associated with biliary tract infection. It is useful in this group of cases both before and after cholecystectomy, especially in the latter instance, as in such a case often it tells one what nothing else can. These cases are relatively rare, but they are very important for, if we can realize how extensive is the involvement of the entire biliary tract before operative procedure has been considered, we may either decide to postpone operation longer, or, instead of the usual cholecystectomy, to advise cholecystostomy with its long period of drainage or in particular instances cholecystgastrostomy (*i. e.*, when severe icterus is accompanied by extensive hepatitis).

The three mentioned diagnostic methods combined with physical examination and the ordinary laboratory procedures (study of blood and urine, etc.), are our main diagnostic standbys. But there are other methods which sometimes are of help: the study of local areas of hyperasthesia, frontal or dorsal pain points, the estimation of pancreatic ferments in the duodenal contents to see if one can secure evidence of an associated pancreatitis, the estimation of bile acids in drainage material, some observers having suggested these are diminished in calculous cholecystitis but not in inflammation without stone. Possibly of much greater value are functional liver tests, for as Graham, McComb, Jackson and others have preached, every cholecystitis with or without stone is associated with inflammation of the liver—mild, moderate or severe. In such lesion this hepatitis may be far more the cause of symptoms than is the gall bladder itself.

In regard to *tests of liver function*, many have been suggested for the liver is very protean in its activities: bile forming, glycogenic, antitoxic, in addition to the *role* it plays in fat and protein metabolism. Really to visualize the liver's condition, theoretically at least, tests based on each of these functions should be utilized.

Unfortunately, few of these special tests are really satisfactory, few are very accurate; but of the commonly used tests, each of them may help a little in certain cases. In our experience, however, in most instances this help often is very little, although the galactose test probably is of more value than are the Van den Bergh, icteric index, bromsulphalein, urobilinogen or the estimation of dye retention in cholecystography by the Graham intravenous method.

It is a great pity that we cannot know better the state of the liver in this group of cases and therefore better plan preoperative and post-operative treatment, for after operations upon the gall bladder, if death occurs, usually it is not postoperative pneumonia nor general peritonitis which is the cause, but is hepatic insufficiency.

With the utilization of all the diagnostic methods at our command, history, physical examination, various laboratory procedures and cholecystography, we believe that we should be able to make a correct diagnosis both as to the presence or absence of pathology as well as its nature and degree in about 90% of the cases.

II. TREATMENT

After the diagnosis has been made, what is the proper method of treatment? Is surgical or non-surgical therapy indicated? And if surgery is decided upon, what is the operation of choice? By the various methods, what are the chances of cure or of relief? What is the percentage of failures and what are the possible complications?

There is an ever-increasing feeling that in the treatment of diseased gall bladders, surgery has been disappointing in a number of cases. Is this feeling justified, and if so what is the reason for failure?

To my mind there is no question that in the very definite, very *severe lesions* of the gall bladder—suppuration, gangrene, perforation, stone—where frequent or severe attacks of gallstone colic take place, surgery is the only procedure to consider. Whether, in the former group, one should operate during the acute stage, doing a cholecystectomy if possible, whether one should wait until that stage is over, confident that even if perforation does occur, the omentum will prevent general peritoneal infection, still is a moot question. Graham, for example, "has not advised an operation on an 'acute gall bladder' for four years and except for the finding of an occasional pericholecystic abscess, which probably represents the perforation of an acutely inflamed gall bladder, has seen only two cases of perforation causing general peritonitis."

Mentzer, on the other hand, says "perforations on the upper aspect of the gall bladder and those that are immediately walled off by the omentum may be operated upon later, but in the present state of our knowledge we apparently cannot diagnose a case of perforation from a gangrene or acute empyema" . . . therefore he advises immediate operation.

Most surgeons agree with the former view, perhaps a smaller but increasing number with the latter view. When surgeons differ, what is a mere internist and diagnostician to believe and to advise? Is it safer to operate or not operate immediately on these acute cases? Are they to be regarded as emergency or semi-emergency operations or as cases where it is wiser to wait until the acute process has subsided (and most of these cases I believe will subside), or is immediate operation indicated?

I feel quite sure that a few cases unquestionably need immediate surgery. I feel equally sure that for no reason that I have been able to determine, this group of cases is increasing; but how to determine this relatively small group, there is the rub! On the other hand, I believe that by a thorough analysis of each case, by having no fixed general rules, by regarding each as an individual problem, by weighing all the factors—the general condition of the patient, the leucocyte count, especially the differential count, the temperature chart, the examination of blood and urine, and intensive clinical study of the patient—usually one can (although not always) decide whether the acute aspects of the case are subsiding or are becoming progressively worse.

There is, of course, no question in my mind that in the progressing group immediate operation is indicated. In the former group, I feel equally sure mortality is likely to be lowered by performing an interval operation after the fulminant acute inflammation has subsided. We must, however, not forget that the symptoms and signs in some of these cases occasionally may be so slight that gangrene and perforation may take place with very few local, and no very striking general, signs or symptoms.

As to the *prognosis* in operations upon the gall bladder: even in those with symptoms of severe infections, usually it is good; if patients weather successfully the immediate operative and post-operative dangers, their subsequent condition usually is excellent. It is rather a wise rule to remember that in abdominal surgery the more severe the symptoms, the more definite the diagnosis and, the more obvious the surgical need, the better are the results obtained.

In the *chronic cases* of cholecystitis, with or without stones, when the symptoms are not fulminating or acute, when the attacks are not severe or frequent, what should be our attitude as regards treatment? Does surgical or non-surgical treatment offer the better prognosis? Should we accept the view of certain surgeons and say that every diseased gall bladder should be removed as early as possible because by so

doing a potential focus of infection will have been eliminated, the associated hepatitis and biliary tract infection usually will quickly subside, it will minimize the possibility of secondary lesions—pancreatitis, diabetes, persistent functional dyspepsia—and the possibility of malignant degeneration will be reduced to a minimum? Or, should one say it is in just this group of cases in which operation should be postponed indefinitely, if possible, because the dangers of waiting are far outweighed by the possible or probable post-operative sequelae? What are these possible sequelae? Among them are post-operative adhesions, a common duct stone, possibly sometimes pushed down into the common duct during the manipulation of operation, either of these often absolutely reproducing the original syndrome or producing a new syndrome often as bad, such as periodic attacks of greater or lesser obstruction or periodic attacks of biliary tract infection or even persistent low grade biliary tract disease, causing symptoms sometimes more severe than the original picture. The fact remains that functional disturbances often remain after gall bladder removal and these have become so well established that they, not the underlying pathology, dominate the picture, or again one must appreciate the fundamental conception that certain of chronic "gall bladder" cases in reality present symptoms far more referable to diseased liver and biliary tract than to the gall bladder alone, the gall bladder playing but a minor role. Here, its removal, even with the compensatory biliary tract dilatation, often brings about no benefit but often real harm by the effect of post-operative adhesions. Perhaps even more important still, is the fact that from these patients we have removed a crutch upon which we may have to lean heavily if the infection of liver and biliary tract does not subside.

It is an argument in favor of cholecystostomy rather than cholecystectomy in certain of this group of cases, because, if the better drainage from cholecystostomy should not clear up the picture, the gall bladder later may be anastamosed to the stomach, thus providing a channel for free permanent drainage—a far wiser and safer procedure than is a long continued drainage through a densely tied-up common duct by means of ordinary catheter or a T-tube or by an attempt to establish a fistula and then transplant it into the stomach. Such operation is, to me, a very wise procedure to consider long before cholecystectomies are done when there is marked evidence of hepatitis or of extensive infection of the rest of the biliary tree. Of course, I am sure that cholecystectomy is by far the best operation in the vast majority of cases. I am equally sure that it is the worst operation in that small group where in addition to gall bladder disease there is evidence of extensive disease of liver and biliary tract as well.

Quite frankly, these cases of chronic disease are not treated with especial success by medical measures and, personally, I should feel far safer if first a cholecystostomy were done to see the effect of its long, free drainage or even if there was performed an immediate chloecystogastrostomy with the object of bringing about permanent drainage.

I feel very strongly that in the case of chronic cholecystitis, unless the operative indication seems very definite, especially if the picture is blurred and the symptoms indefinite and where we lay our diagnosis more on the altar of cholecystography than on that of symptomatology, and in cases where there is evidence that the symptoms are increased by an unstable *psyche*, it is wiser to postpone operation sometimes indefinitely, sometimes until we have proven definitely that all other measures are ineffective.

In this group of cases, what non-surgical measures can we offer? What is their chance of relieving the symptoms in whole or in part, in bringing about a clinical cure even if not an anatomical cure, because of course no medical measures can dissolve gallstones, cause adhesions to disappear or make new a mucous membrane or bladder wall which has been chronically thickened by disease? What are the principles governing the medical treatment of these cases? What can it hope to do? Is it likely to be successful in a considerable proportion of the cases? Can it produce a clinical cure in many cases? Can it relieve a number of patients so that they are relatively well? Will it be so effective that fever or jaundice or evidences of periodic, common duct obstruction or attacks of gallstone colic will not recur? Or, if they do, will they be of so much less intensity and severity and at so much longer intervals that the patient will be satisfied? Will the underlying pathology be improved or at least not be progressive?

As I see it, our two main objects in medical treatment are: first, to minimize the chances of reinfection of the biliary tract, and second, to promote free biliary drainage. The first goal sought is brought about by keeping mouth, teeth, tonsils and sinuses in as perfect condition as possible; by avoiding in the diet mechanical, chemical or thermic irritants, highly seasoned foods, rich foods, excessively coarse foods and for most patients, probably alcohol, so that the chance of gastritis and duodenitis is reduced to an irreducible minimum; to avoid constipation or diarrhoea so that there is a minimal chance of infection from the colon.

The weight of evidence certainly is in favor of the lower bowel playing a considerable infective *role* in these cases; some clinicians believe that rarely is there gall bladder infection without a preceding colitis. In the majority of patients, appropriate diet with large amounts of the softer fruits and greens, the elimination of astringent foods and the installation of a regular habit is all that is necessary, with, of course, the general hygienic measures so necessary to every bodily function—plenty of sleep, a normal amount of exercise, fresh air and play, and as much freedom from worry as is possible in this vale of tears. In many cases, this regime is all that is necessary, but in some patients, laxatives have to be used. Unquestionably it is true that in the vast majority of cases, recurrences of symptoms of biliary tract disease are due to reinfection; therefore it is essential to minimize this possibility by every means at our command. There is, however, very little evidence that specific disinfection of the gall bladder or biliary tract, as Hurst has suggested by the use of methenamine, is possible, for although the drug is eliminated in the bile, it is in such small amount and so much diluted as to make me feel that it cannot have any appreciable bactericidal effect.

As to the second requisite in treatment, the promotion of free biliary drainage, we have many means at our command but none so good as that method most physiologic of all, the utilization of the normal gall bladder emptying by the intake of food. Frequent feedings, a proper non-irritating diet, with large amounts of those substances especially effective in emptying the gall bladder, such as butter, cream, olive oil and especially egg yolk, these foods to be given in large amounts even if gallstones are present, for the evidence is distinctly against their playing any definite *role* in gallstone formation. In my experience the only justification for their elimination from diets is when jaundice is present. This is the fundamental dietetic procedure. It is really quite remarkable how often olive oil, before meals or on waking, or one or two raw eggs at night will bring about a rapid emptying of the gall bladder and often act as a gentle laxative as well. We use these foods in the cholecystographic test; why be afraid of them in our treatment of disease?

All the salines help—a morning dose of phosphate of soda, magnesium sulphate, the "Bourget mixture," ordinary table salt or lemon juice and soda, or perhaps better still a smaller dose shortly before each of the three meals, given preferably in hot water, often is singularly effective. It is well to remember that magnesium sulphate is not a specific, is not *sacro sanct*, that all salines have the same effect to a greater or lesser degree. Also one should not forget that magnesium sulphate by mouth in capsules or in saturated solution, is just as effective a cholagogue as when administered through that most unphysiologic of instruments, the duodenal tube. It may be good psychotherapy to use the tube in certain cases; it certainly is not indicated as a physical agent and I

for one prefer to give my suggestive treatment, if that seems necessary, by more rational, less expensive and less time-consuming methods.

These are our two main methods of attack, and while, in certain cases, antispasmodics such as belladonna, or mild sedatives such as luminal or the bromides, or hydrochloric acid if the gastric acid is absent, may help; it is upon these two procedures that we must place our main reliance.

How many cases can we help by these methods? Few, if any, of the fulminating or acute lesions, a fair proportion of cases with gallstone colic, a large number of cases of chronic cholecystitis with or without stones. How large a percentage of success in this large group? We cannot say, for practically it is impossible in the proportion of cases so treated to determine how many have been helped greatly, how many have been cured clinically or how many have been complete failures. I have a feeling, however, that a very large proportion of cases may be helped by such method of treatment outlined if the patient is willing to follow the treatment in principle for a long period of time, perhaps even indefinitely. In my own practice I have a very large number of patients who have been comfortable and symptom-free for long periods of time by such procedures alone: even cases with demonstrable stones or with definite evidence from an X-ray viewpoint at least of considerable gall bladder pathology; cases in which there is no evidence of any progressive damage being done to liver, biliary tract, gall bladder or pancreas by such an expectant therapy and where for long periods there have been no recurrences of acute or subacute infection, enlargement of the liver or of any other finding suggesting any damage to liver function. But to repeat, here as in any case of chronic disease elsewhere, the patients must follow certain general directions as regards diet and personal hygiene if they hope to remain symptom-free.

What is the percentage of cures of these cases which are treated surgically? Ask the surgeon and he will tell you from 85% to even 90% or more. But this, I am sure, is far too high, for the surgeon is an incurable optimist: often it is impossible for him to know of his failures, for when there are failures, the patients rarely return to the surgeon for advice but go to an internist or to another surgeon.

In our Clinic at the Johns Hopkins Hospital something more than one-quarter of our operated patients—subjects chosen with great care as fit for surgery by a conference of surgeons and clinicians—come back to us complaining of the same symptoms or different symptoms, but complaining! Dr. Howard* will report in complete detail the results of the analyses of 81 cases in our private practice on whom I had advised surgery and where it was possible to find out exactly what the ultimate results of the operation were. On 63 of these cases cholecystectomy had been performed, on 13 cholecystostomy, on one cholecystogastrostomy, on one choledochotomy, and on the remainder, the separation of adhesions. In 4, I had a cholecystectomy done following an earlier cholecystostomy.

Our surgical mortality was 4.7%, a little higher than the 3.6% of Eusterman's series in 804 cases. Of our series, 59% had complete cure, relative cure or relief from the disagreeable symptoms; but this leaves the rather striking figure of 41% in which operative treatment was unsuccessful—a figure sufficiently high to make us very careful in our decision in each individual as to whether surgical or non-surgical treatment is the better procedure.

I, for one, therefore, cannot feel that surgery should be indiscriminately advised for all cases of gall bladder pathology. It has a definite mortality; it has a considerable proportion of failures; it has many post-operative possibilities which may make the second state of the patient the same as, or even worse than, the first.

Vide infra, this issue of *The Journal*.

RECAPITULATION

May I, at the risk of repetition, again stress my belief? It is that, while in those cases where the clinical picture is a severe one—a very clear cut one, one with very marked local or general symptoms—surgery is the only safe reed upon which to lean. In the milder, less definite and more chronic type of case, it seems better, in view of our present knowledge, first to try the simpler and perhaps safer medical measures. Many cases so managed remain symptomatically cured if they are willing to follow a certain *regimen*, and this, not an onerous one; some, and not a negligible portion, may later have to have recourse to surgery either because they get tired of such a *regimen* or because they do not get sufficient relief from it to make the physician feel that he is justified in continuing it.

CONCLUSION

In this paper I have tried to bring before you the results of my experience in this field, my *credo*, if you will, and to ask you to share with me certain beliefs that have, through many years, gradually crystallized in my mind and which have helped me in my attempt to attack this very difficult problem in the way that is best for patient and for doctor.

I am sure that it is wrong to consider the gall bladder as a separate entity and not as a part of the entire biliary tree, although in a considerable proportion of cases, the major portion of the pathology is concentrated there and it is in this group of cases where surgical attack upon the gall bladder is likely to be most successful. I am convinced that, in analyzing the symptoms, we must determine how many are referable to the gall bladder itself, how many to liver, ducts and biliary tract, for on the results of such analysis, must rest our decision as to medical or surgical treatment; and, if the latter is decided upon, what is the best operative procedure?

I am quite convinced that cholecystectomy is the operation of choice in the vast majority of cases in which surgery is indicated, and, that in a good many of these cases, complete relief may be obtained by the removal of the gall bladder. I am equally convinced that where there is evidence of extensive liver and biliary tract infection as well, it is far wiser, if surgery is to be done, to employ cholecystostomy, possibly followed later by cholecystectomy or cholecystogastrostomy.

I have touched upon the physiological basis for medical and dietetic treatment and its simplicity and its success in a fair number of chronic cases if carried out conscientiously, but I have tried not to over-emphasize its value because surgery must be utilized in most of the severe and many of the milder cases. Finally (for after all what is the value of treatment if diagnosis is not correct?), I have tried to preach the doctrine of thoroughness in reaching one's final conclusions as to the underlying pathology: I have insisted upon the absolute necessity of a careful history of the case as well as the utilization of all the laboratory methods at our command. I have pointed out the difficulties in diagnosis in this field because of the striking tendency of the gall bladder to mirror symptoms due to disease elsewhere and in turn to be the cause of referred symptoms.

To me, this will always be a fascinating field, a field beset with many difficulties, a field in which often we must grope rather blindly for a while, but one which I feel sure will become easier and easier of exploration if we attack each individual case thoroughly and scientifically—without prejudice and without bias—and if we try to learn as much, or more, from our failures than from our successes.

LATE MANIFESTATIONS OF AMEBIASIS

By

R. W. MENDELSON, M.D.

ALBUQUERQUE, NEW MEXICO

THE recent epidemic of amebiasis emanating from Chicago, has resulted in numerous excellent articles on the affection. By now, the medical profession should be well-versed in the symptoms and the treatment of amebic dysentery *per se*.

It is reasonable to suppose that some of the acute instances will become chronic and that many infected persons will not develop dysentery symptoms. It is this type of infection—the chronic dysentery case and the latent infection—which may, later on, develop complications of a serious nature. It is well that one consider briefly the late manifestations of amebiasis in order that he may be prepared to make a proper diagnosis and institute adequate treatment.

The following classification of the clinical and pathological manifestations of amebic infection, in the order of their frequency, is derived of our ten years' experience in the tropics of the Far East.

I. Typical amebic dysentery
 (a) Acute
 (b) Chronic

II. Extensive ulceration with massive hemorrhage

III. Liver abscess

IV. Intestinal obstruction
 (a) Due to stricture
 (b) Due to tumor formation

V. Intestinal perforation
 (a) Intraperitoneal with peritonitis
 (b) Extraperitoneal with fecal fistula

VI. Pulmonary and other rare abscesses.

As stated above, *typical acute amebic dysentery* has been dealt with at length in numerous articles both in the medical and lay press. It might be stated that the country's population is at the present time "dysentery conscious." This sudden awakening to the seriousness of the infection on the parts of both physician and layman will reveal many cases of chronic amebic dysentery that have been treated as non-parasitic "ulcerative colitis." I have found this type of case, severe ulcerative, very subject to massive hemorrhage. This complication, although immediately alarming, is not so serious as would at first appear. On the other hand, continuous loss of blood, although it may not be noticed by the patient, eventually leads to serious secondary anemia and loss of resistance. In the treatment of chronic dysentery with extensive ulceration, it is advisable, in addition to the specific treatment, to administer some preparation of calcium. The scientific administration of such drug materially assists in the healing of the ulcerations and the control of bleeding. Too often these patients are treated only for their amebic infection while the general condition is neglected.

Liver abscess is one of the most common and serious manifestations of amebic infection especially in the Tropics. The relationship between liver abscess and amebic dysentery is very similar to that of tabes dorsalis and primary syphilis. In both instances, the unfortunate patient may be quite innocent of the fact that he ever suffered an infection. This, of course, is not absolute, but not infrequently the patient with a liver abscess never has had dysentery; we all have seen patients with tabes who have never been aware of the fact that they at one time were infected with syphilis.

The diagnosis of amebic abscess of the liver is not difficult once a tumor mass presents itself. When the patient reaches this stage of the disease, the treatment is of course surgical, combined with the usual medical therapy and general care. Our aim should be to diagnose the condition before it has made such extensive progress. We should be suspicious when a patient complains of vague hepatic distress, slight elevation of temperature, a degree of leukocytosis and the history of exposure particularly with special reference to the Chicago outbreak. These patients should have the advantage of a thorough intestinal analysis, primarily for the detection of the cysts of *endameba hystolytica*. In some patients, it is possible to abort an incipient liver abscess, if the condition is diagnosed early and treated thoroughly.

The surgical treatment of a liver abscess does not end with the discovery of the characteristic abscess material. Not infrequently these abscesses are multiple and may or may not communicate with each other. An attempt should be made to locate and drain them all. Before these patients are operated upon they should be saturated with sugar for several days during which time anti-amebic medication should be pushed.

Intestinal obstruction was less frequently observed by the author than was liver abscess. Obstruction due to stricture,



Figure 1—Amebic abscess of the liver.

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Figure 2—Amebic abscess of the liver ruptured into lung and draining through mouth.

(Figure 4) incident to healing ulceration, is much more common than is obstruction due to tumor formation (Figure 5). It has been my observation that patients suffering from obstruction, due to stricture, usually give a very definite history of dysentery. This, of course, is to be expected since their intestinal infection has been active and not passive.

The pathology in these cases can be fairly well anticipated when there is a history of dysentery and one finds amebae or their cysts in the stools. Otherwise, the usual diagnosis is malignancy especially when one deals with obstruction due to tumor formation. Amebic granuloma is not a frequent finding. The case illustrated (Figure 5) was a patient over fifty years old, who came to the hospital complaining of complete obstruction for more than a week. The diagnosis was "malignancy." The operative procedure proved fatal and a tumor mass presented as shown by the Figure. Sections of the tumor revealed *endameba histolytica* in the tissue; the stool, post-mortem, revealed cysts of the same protozoan. (Figures 6 and 7 are microscopic sections of Figure 5.)

Intestinal perforation. We have not found such to be a common complication of amebic dysentery. Intraperitoneal perforation with peritonitis practically always is fatal. There is little to be said about diagnosis or treatment. The patient presents himself with an "acute abdomen" and the operative procedure is an emergency one. The exhibition of anti-amebic medication combined with free surgical drainage are the only procedures one can carry forward.

Extraperitoneal perforation accompanied by fecal fistula (Figure 8), is a rare complication. This particular patient from which our specimen was obtained insisted that he had never suffered from dysentery. It is possible that he controlled his tendency to dysentery by the large amounts of opium which he smoked. The defect in his colon is shown in Figure 9. The tissues of the abdominal wall immediately surrounding the fistula were heavily infected with amebae. They could be recovered from under the skin edges and from the muscles of the abdominal wall.

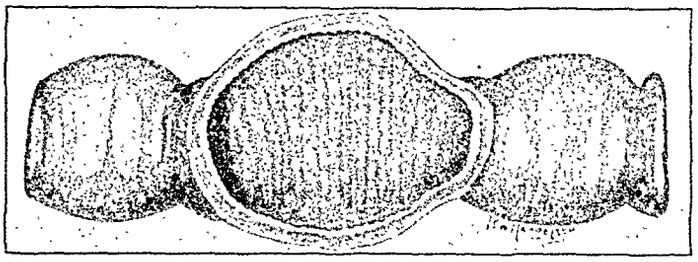


Figure 9—Illustrating defect in bowel in extra-peritoneal perforation.

This type of case is treated best by side-tracking the intestinal flow through a colostomy and then instituting thorough anti-amebic medication.

Pulmonary abscess is rare. One must bear in mind the fact that the lung may become infected *via* the hepatic veins and not necessarily as an extension process from abscess of the liver. In Figure 2 there is detailed an amebic abscess of the

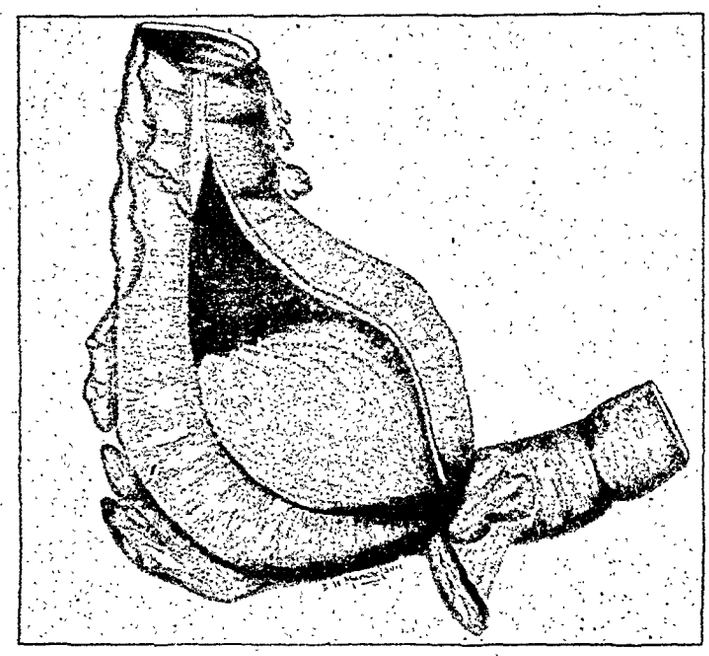


Figure 5—Amebic granuloma of cecum.

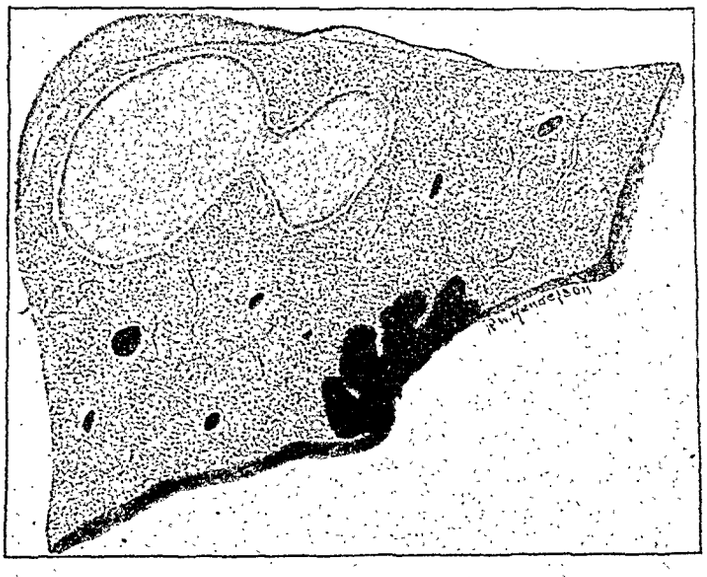


Figure 3—Amebic abscess of the liver.



Figure 8—Intestinal perforation.

liver which had ruptured into the pleural cavity. When examined, this patient was expectorating sputum laden with amebae. Actually he was draining his own liver abscess through his mouth. The extent of his lung involvement I could not determine since he recovered sufficiently to leave the hospital after free drainage and rather severe medication.

The diagnosis of true pulmonary abscess should not be difficult as a microscopic and cultural examination of the sputum reveals its nature quickly. These patients should recover, if there is free bronchial drainage and anti-amebic therapy is pushed.

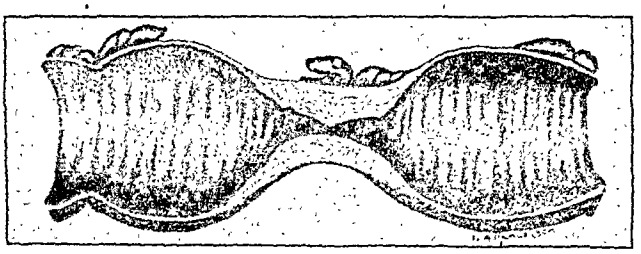


Figure 4—Stenosis of bowel incident to healing ulceration.

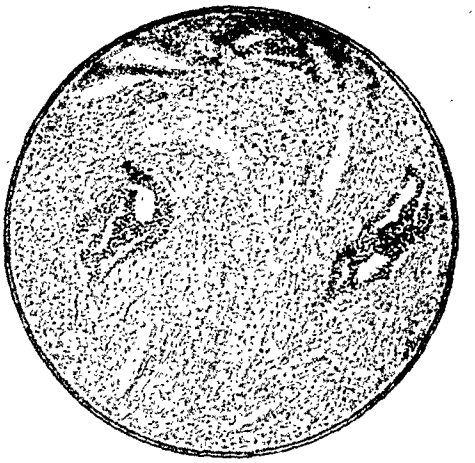


Figure 6—Amebic granuloma—low power.

I have never observed brain and other abscess formation. With regards joint involvement, mentioned by some authors, I have not been able to diagnose an instance. I do not know of a case of articular amebiasis diagnosed in the Far East.

In the medicinal therapy of amebiasis I do not believe we have yet found an agent which replaces emetine. Especially does this apply to the initial period of management of dysentery-form symptoms. I have found that emetine, combined with one of the many newer anti-amebic, arsenic- or iodine-rich preparations, offers the patient the best hope of recovery. Of the arsenicals, personally the author favors yatren.

It behooves every medical man to keep in mind the many complications of amebiasis and to insist on stool studies in every suspicious case; and not *one* stool examination but at least six specimens and many smears (unstained and stained) from each stool. No stool should be considered ameba-free without negative cultures in addition to direct stool examinations.

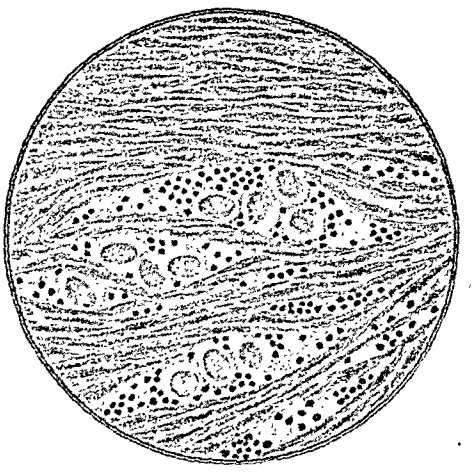


Figure 7—Amebic granuloma—high power, showing amebas in the tissues.

COMPLEMENT FIXATION TEST FOR AMEBIASIS*

(PRELIMINARY REPORT)

By

EMIL WEISS, M.D.

and

LLOYD ARNOLD, M.D.

CHICAGO, ILLINOIS

THE recent experience with amebiasis in Illinois has raised many problems in the minds of public health authorities. One problem which has faced the State Department of Public Health has been a practical method of detecting infectious carriers or cases. Any control method necessitates a knowledge of the reservoir of the causative agent before practical means of preventing the spread of this parasite effectively can be instituted. The repeated microscopic examinations of the stools of contacts, food handlers, etc., have not proved to be a practical procedure. There are few properly trained parasitologists; the method is slow, cumbersome and expensive when viewed from the standpoint of economical and practical public health laboratory procedures.

The cultural method of diagnosis offered a better procedure for practical public health purposes. But even this method requires considerable technical assistance and a great deal of special culture media. If repeated examinations are made upon the same subject, the laboratory methods become cumbersome and expensive. The direct examinations of the feces for trophozoites and encysted forms are the methods of choice for diagnosis in clinical work.

We are reporting here a complement fixation reaction for amebiasis, which should be considered by public Health laboratories. The method could be of value in making surveys of a large number of food handlers to determine the relative complement fixing antibodies in the blood. Direct stool examination could then be carried out on a limited number of suspects.

There are several complement fixation methods (Craig†[3, 4] and Heathman[9]), recommended for amebic dysentery. Most of them appear as special applications of certain Wassermann-like procedures, using amebic extracts as antigens (Craig[1, 5], Menendez[8], and Sherwood[10]). The complement fixation test for amebic dysentery is not so sensitive as is the Wassermann test for syphilis. This is generally conceded to be true because of the difficulties of preparing reliable antigens and also due to the small amount of antibodies in serum of amebiasis patients. Some forms of colitis without clinical symptoms of amebic dysentery cause, in a certain percentage of cases, positive complement fixation (Craig[6, 7]). Whether these returns represent obscure, undiagnosed cases of amebic dysentery or only non-specific positive reactions, remains for the time unsettled.

The following procedure represents an attempt to increase the sensitiveness of the test by elimination of superfluous steps which complicate the procedure without contributing toward the reliability of the test. A few new steps have been introduced which increase the specificity of the reactions.

THE TEST

Apparatus and glassware. On account of uniformity of temperature, the water bath is preferred to the use of the incubator. Glassware such as pipettes and tubes are recommended the same as for any complement fixation test. The use of a shaking machine, in order to insure a thorough mixture of reagents, especially preceding the second incubation, is recommended.

THE ANTIGEN.—I. Preparation of the antigen. The 48-hour growth from ten culture tubes of *endameba histolytica*, using satisfactory culture media (Cleveland and Collier,[11]) is transferred to centrifuge tubes and centrifuged at high speed. The supernatant fluid then is removed, the sediment resuspended in normal saline and again centrifuged. The procedure is repeated until the supernatant fluid appears quite clear and colorless. The contents of the centrifuge tubes then are uniformly spread over a glass plate or a wide dish and dried overnight in an incubator at 37° C. The following day the residue is scraped off with a knife and placed in a wide tube or flask and covered with 50 c.c. of absolute alcohol. The extraction is carried on for 48 hours at 55° C. in a water-bath. The tube or flask containing the extract is concentrated by evaporation of the alcohol, until it assumes a distinctly yellow color. The evaporation then is interrupted and 0.1 c.c. of the extract removed from the tubes and diluted with 0.9 c.c. saline. If the addition of saline to the extract causes sufficient opalescence the evaporation is discontinued; otherwise the evaporation is continued until the extract, when diluted with saline shows distinct turbidity. The extract is then filtered and preserved in tightly stoppered bottles. Rubber stoppers are preferred. The extract is now ready for titration.

II. Titration of the antigen. Twenty Wassermann tubes are placed in two rows in a rack. Increasing amounts of the extract .05, .1, .2, .4, .6, .8 c.c. diluted 1:10 and .5, .6, .7, .8 c.c. diluted 1:5 are placed in the ten tubes of the front row, and the same amounts in the corresponding ten tubes of the back row. Normal saline is added to each tube to make up .8 c.c. Each tube of the front row receives 1 c.c. of an inactivated negative serum and each tube of the back row receives 1 c.c. of a strong positive (amebic) serum. Each tube of both rows receives 0.1 c.c. of a 50% complement. The tubes are shaken vigorously and placed in a water bath for ½ hour at 37° C. After the incubation 5 units of amboceptor in .5 c.c. saline and 0.1 c.c. of a 25% suspension of washed sheep blood cells are added to each tube. The tubes are again shaken vigorously and placed in a water bath for ½ hour at 37° C. The results are then read. The largest and smallest amount of the antigen giving complete inhibition with a positive serum and hemolysis with a normal serum is determined. *The amount of antigen midway between the largest and smallest specific dose is then selected as the antigenic dose.* (See Table I.)

TABLE I.

Titration of the Antigen.

Tubes	Antigen	Normal Saline (.85%)	Inactivated Serum (½ hr. at 55° C.)	50% Complement	1st Incubation	5 Units Amboceptor	25% Sheep Red Blood Cells	2nd Incubation
1	.05 c.c. 1:10	.75 c.c.	Normal 1 c.c.	.1 c.c.	Shake vigorously and place the tubes in water-bath at 37° C. for ½ hour, then add:	.5 c.c.	.1 c.c.	Shake vigorously and place the tubes in water-bath at 37° C. for ½ hour, then read the results.
2	.1 c.c. 1:10	.7 c.c.	Normal 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
3	.2 c.c. 1:10	.6 c.c.	Normal 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
4	.4 c.c. 1:10	.4 c.c.	Normal 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
5	.6 c.c. 1:10	.2 c.c.	Normal 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
6	.8 c.c. 1:10	0 c.c.	Normal 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
7	.5 c.c. 1:5	.3 c.c.	Normal 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
8	.6 c.c. 1:5	.2 c.c.	Normal 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
9	.7 c.c. 1:5	.1 c.c.	Normal 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
10	.8 c.c. 1:5	0 c.c.	Normal 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
11	.05 c.c. 1:10	.75 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
12	.1 c.c. 1:10	.7 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
13	.2 c.c. 1:10	.6 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
14	.4 c.c. 1:10	.4 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
15	.6 c.c. 1:10	.2 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
16	.8 c.c. 1:10	0 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
17	.5 c.c. 1:5	.3 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
18	.6 c.c. 1:5	.2 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
19	.7 c.c. 1:5	.1 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
20	.8 c.c. 1:5	0 c.c.	Amoebic 1 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	

*From the Department of Bacteriology and Preventive Medicine, University of Illinois, College of Medicine and the Research Laboratories of the Illinois Department of Public Health, Chicago.

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†To Col. Craig the medical profession is indebted for initially devising the first practical method for a complement fixation test in amebiasis. Despite years of neglect of Col. Craig's technique and failure of laboratory workers and clinicians to appreciate the significance of his pioneer efforts, the doughty Colonel "stuck to his guns." It is a pleasure, nay, a duty, here to express appreciation of the epochal efforts of Col. Craig—one of our country's most distinguished investigators and scholars.

The patient's serum. The sera are inactivated for ½ hour at 55° C. Fresh sera immediately are inactivated after separation from the blood clot, and then preserved in the ice-box until used. A mixture of several normal sera should be used as a negative control. In the absence of strong positive sera, immune serum (rabbit) should be used. The immune serum is prepared by intravenously inoculating rabbits twice weekly with saline washings of ameba cultures in increasing amounts. Six inoculations usually suffice and the rabbits are bled two weeks after the last inoculation. Smallest dilutions of the immune serum still giving strong positive reactions should be used in the absence of strong positive human sera.

The complement. A mixture of sera of several guinea pigs is preferred to the use of the serum of a single guinea pig. Otherwise the same rules apply as generally practiced in the Wassermann test. One-tenth of a cubic centimeter of a 50% dilution of complement is used instead of a .5 c.c. of a 10% dilution in order to allow a greater relative volume for other reagents.

Red blood cells. Sheep cells were selected in preference to human blood cells, the former being more available in most of the laboratories where Wassermann tests are performed. The preparation of the blood cells for the test otherwise is the same as in any other complement fixation test. One tenth of a cubic centimeter of a 25% suspension of red blood cells is used instead of .5 c.c. of a 5% suspension in order to allow more space for other reagents.

Sheep blood hemolysin (amboceptor). Amboceptor is prepared in the same manner as that used in the Wassermann test. The amboceptor is titrated against fixed amounts of complement. Increasing dilutions of the amboceptor are prepared and .5 c.c. of each dilution is placed in a series of ten tubes. To each tube 1.3 c.c. saline and .1 c.c. of 50% complement are added. The tubes are shaken and placed in a water-bath for ½ hour at 37° C. After the incubation .5 c.c. of saline and .1 c.c. of a 25% suspension of sheep cells are added to each tube. The tubes then are shaken and placed for a second ½ hour incubation in the water-bath at 37° C. *The highest dilution of the amboceptor causing complete hemolysis is called one unit.* Five units of the amboceptor are used for the antigen titration and the main test. The double incubation in the amboceptor titration is intended to expose the complement to the incubator temperature for the same length of time as in the antigen titration and the main test. The amboceptor should be titrated each time the complement fixation test is performed. (See Tables II and III.)

TABLE II.

Preparations of Amboceptor Dilutions.*

Tubes	Amboceptor	Saline	Amount of amboceptor - saline mixture	Dilution
1	.5 c.c. 1:100	2.0 c.c.	2.5 c.c.	1:500
2	2.0 c.c. 1:500	2.0 c.c.	4.0 c.c.	1:1000
3	1.0 c.c. 1:1000	1.0 c.c.	2.0 c.c.	1:2000
4	.5 c.c. 1:500	1.0 c.c.	1.5 c.c.	1:3000
5	.5 c.c. 1:2000	.5 c.c.	1.0 c.c.	1:4000
6	.1 c.c. 1:1000	.4 c.c.	.5 c.c.	1:5000
7	.1 c.c. 1:1000	.5 c.c.	.6 c.c.	1:6000
8	.1 c.c. 1:1000	.6 c.c.	.7 c.c.	1:7000
9	.1 c.c. 1:1000	.7 c.c.	.8 c.c.	1:8000
10	.1 c.c. 1:1000	.8 c.c.	.9 c.c.	1:9000

*Additional dilutions of amboceptor can be prepared, if necessary.

TABLE III.

Amboceptor Titration.*

Tubes	Amboceptor	Saline	50% Complement	1st Incubation	Saline	25% Sheep Red Blood Cells	2nd Incubation
1	.5 c.c. 1:500	1.3 c.c.	.1 c.c.	Shake vigorously and place the tubes in water-bath at 37° C. for ½ hour, then add:	.5 c.c.	.1 c.c.	Shake vigorously and place the tubes in water-bath at 37° C. for ½ hour, then read the results.
2	.5 c.c. 1:1000	1.3 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
3	.5 c.c. 1:2000	1.3 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
4	.5 c.c. 1:3000	1.3 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
5	.5 c.c. 1:4000	1.3 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
6	.5 c.c. 1:5000	1.3 c.c.	.1 c.c.		.5 c.c.	.1 c.c	
7	.5 c.c. 1:6000	1.3 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
8	.5 c.c. 1:7000	1.3 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
9	.5 c.c. 1:8000	1.3 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	
10	.5 c.c. 1:9000	1.3 c.c.	.1 c.c.		.5 c.c.	.1 c.c.	

*Additional dilutions of amboceptor can be prepared, if necessary.

THE MAIN TEST. Racks with two rows of tubes are used. The tubes of the first row receive the titrated amount of antigen, while the tubes of the second row receive saline instead of antigen and serve as serum controls. Each tube of the first and second row receives 1 c.c. of the respective serum. The last tube in the first row receives, instead of 1 c.c. serum, an equivalent amount of saline; this tube serves as antigen control. All tubes then receive saline to make up 1.8 c.c. and then .1 c.c. of 50% complement is added to each tube. The tubes are then vigorously shaken and placed in the water-bath for ½ hour at 37° C. After the incubation five units of amboceptor in .5 c.c. saline and .1 c.c. of a 25% suspension of sheep red blood cells are added to each tube. The tubes are again vigorously shaken and placed in the water-bath for ½ hour at 37° C. The results are then recorded. (See Table IV).

TABLE IV.

The Main Test.

Tubes	Antigen	Normal Saline (.85%)	Inactivated Serum (¼ hr. at 55° C.)	50% Complement	1st Incubation	5 Units Amboceptor	25% Sheep Red Blood Cells	2nd Incubation
1	Titrated amount	q.s. .8 c.c.	Unknown 1 c.c.	.1 c.c.	Shake vigorously and place the tubes in water-bath at 37° C. for ½ hour, then add:	.5 c.c.	.1 c.c.	Shake vigorously and place the tubes in water-bath at 37° C. for ½ hr., then read the results.
2	0	"	"	"		"	"	
3	Titrated amount	"	Normal 1 c.c.	"		"	"	
4	0	"	"	"		"	"	
5	Titrated amount	"	Amoebic 1 c.c.	"		"	"	
6	0	"	"	"		"	"	
7	Titrated amount	q.s. 1.8 c.c.	0	"		"	"	

CONTROLS. 1. Serum-controls. Each serum including the positive and negative control should have a serum control. All serum controls should give hemolysis. *2. Antigen control.* This control should show hemolysis; inhibition of hemolysis would indicate too large an amount of antigen used in the test. *3. Positive control.* Should always show complete inhibition of hemolysis. *4. Negative control.* Should show hemolysis. (See Table IV.)

READING OF RESULTS. After the second incubation, the controls are examined before the unknowns. In the latter, the tubes showing the same turbidity as before the second incubation are interpreted as strongly positive (+ + + +), tubes slightly less turbid are read as positive (+ + +), and tubes showing only slight turbidity are called weakly positive (+ + or +) respectively. Tubes perfectly transparent are interpreted as negative. The test is repeated with sera showing doubtful reactions.

RESULTS

Tables V and VI give a summary of our results in amebiasis in man. Eight cases of acute and 19 cases of chronic amebiasis, as well as 61 carriers, were studied. Blood samples were obtained and the results were later compared with the

TABLE V.

Summary of Observations Upon Patients.

		Four Plus	Three Plus	Two and one Plus	Negative	Total
Acute Amebiasis	Number Cases	3	1	2	2	8
	Number Feces Positive	3	1	2	1	7
Chronic Amebiasis	Number Cases	12	1	2	4	19
	Number Feces Positive	12	1	1	2	16
Amebic Carriers	Number Cases	21	15	6	14	61
	Number Feces Positive	21	15	4	0	40
Wassermann positive Sera (Syphilis)		5	1	3	218	227
Other diseases (Wassermann negative)		0	2	1	326	329

feces findings and the type and duration of treatment. The results of treatment on our small series show that the stool becomes negative before the complement-fixing antibodies disappear from the sera. The discrepancies between the feces examinations for parasites and the serological blood tests are found in the weakly positive group who have been treated and who are becoming feces negative.

TABLE VI.

Resume of Results of Complement Fixation and Feces Examination for Amebiasis.

Complement fixation antibodies in sera	Feces Positive	Feces Negative
Strongly positive four plus and three plus	53	none
Weakly positive two plus and one plus	7	3
Negative	3	17

DISCUSSION

Rabbits were immunized by intravenous injections of saline suspensions of *E. histolytica* obtained from cultures. The complement fixing antibodies are not produced in high concentration even when large amounts of antigen were repeatedly introduced by the intravenous route. This led us to conclude that the use of the standard 0.1 c.c. of sera for complement fixation would not be practical. We then adjusted our set-up so as to have 1.0 c.c. of sera and concentrated the other reagents. The system remains otherwise the same; the patients sera make up 40% of the volume of the tube. The complement used is a 50% concentration; the sheep cells are in a 25% suspension, both to reduce volume and allow more space for the sera which is usually very low in complement fixing antibodies. The preparation of the antigen is based upon sound principles of serological experiences in the Wassermann tests. The lipoids are extracted and the alcoholic solution concentrated by evaporation to the desired concentration. While the material in this paper was in process of being analyzed and recorded, we have found that the lipoidal antigen described above can be used to produce rabbit antisera. This antigen is less toxic and equally antigenic as whole cultures of the *E. histolytica*.

The greatest deviation from other complement fixation tests in this procedure is the use of large amounts of patients' serum. (1 c.c. of the total volume of 2.5 c.c. = 40%). The risk of nonspecific reactions can be fully avoided by the use of proper controls. The advantage and the increased sensitiveness of this arrangement is self-evident. Another advantage introduced in this test is the preparation and titration of antigens. Fewer cultures are required, the time of extraction is shortened by extracting the lipoids at higher temperature; the finished antigen can be further adjusted by evaporation or dilution with absolute alcohol. The triple titration of antigens for antigenic, inhibitory and hemolytic properties is reduced to a single titration. This titration includes the antigenic and inhibitory properties of the extract but not the hemolytic properties. All alcoholic antigens constantly possess hemolytic properties in amounts larger than do those which cause inhibition of hemolysis. Once the inhibitory amounts of an antigen are determined, it is evident, that the hemolytic amounts of the antigen will be larger than those found to be inhibitory. Therefore a special titration of an antigen for hemolytic properties has only theoretical interest, but no practical value.

We do not desire, in this brief preliminary communication, to discuss the question of the use of a mammalian organ lipoid extract possessing broad protozoan antigenic properties for the Wassermann and Kahn tests. We are offering this report at this time because our technic can be repeated in any serological laboratory and can serve as a rapid, practical and inexpensive method of separating those individuals with complement fixing antibodies in their blood and these can then be further examined by any desired procedure. The antigenic properties of lipoids of various protozoa, bacteria and fungi are being investigaged in this laboratory.

SUMMARY

A complement fixation test for *endameba histolytica* has been devised which offers the following advantages:

1. Increased sensitiveness, due to the use of larger amounts of patients' serum.
2. A simplified preparation and titration of the antigens.
3. A more adequate titration of the amboceptor.

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LAMBLIASIS SIMULATING CHOLELITHIASIS*

REPORT OF TWO INSTANCES

With Review of Pertinent Facts Relative to the Clinical and Pathological Significance of *Lamblia* in the Biliary Tract and in the Bowel

By

MEYER GOLOB, M.D.
NEW YORK CITY, NEW YORK

THE incidence of *Lamblia* (Giardia) infestation of the upper intestinal tract has been noted increasingly since the World War. In a number of instances the parasites have been found in the duodenum and the gallbladder. In this location, it is claimed that they are capable of causing an inflammatory reaction in the mucosa.

The two instances here reported are of unusual interest because the *Lamblia* infestation was associated with a symptom-complex closely resembling that of cholelithiasis. The protozoic association was established by detecting *Lamblia* (Giardia) in the biliary aspirates. The first instance is of further interest by reason of the fact that neo-arsphenamine therapy provoked an arsenical dermatitis.

CASE 1.—Mrs. L. G., age 37, married 15 years, *nullipara*, was referred by Dr. Arnold Sturmdorf, May 1931. Her sterility had been ascribed to a sharply anteflexed uterus. Previous personal history was negative

*From the Gastro-intestinal Department of the New York Homeopathic Medical College and Flower Hospital.
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except for typhoid fever at the age of ten. For the past twelve years she had complained of a heavy feeling in the epigastrium, "a feeling of something which necessitates holding that region with my hand," presumably for relief.

The following were the cardinal features of the *presenting symptomatology* one year after the onset of the first attack in May, 1931: A clinical picture descriptive of the gall-bladder-dyspepsia syndrome was evidenced by nocturnal occurrence of biliary "colic" attacks with characteristic radiation of pain, which attacks required hypodermatic injection of morphine. The patient had twice been investigated roentgenologically in two of the largest medical clinics in New York City. Cholecystography repeatedly failed to visualize the viscus. Surgical intervention was urgently advised at both institutions. Except for fatigability, there were no symptoms referable to cardiovascular, renal, pulmonary or endocrine systems.

The physical findings essentially were negative except for loss of thirty-five pounds of weight since May, 1930. Neurological, rectal digital and chest fluoroscopic examinations were negative. Roentgenologic investigation of the gastroenteric tract showed no abnormality other than a persistent shallow defect or drawing in of the outer aspect of the duodenal bulb and a markedly spastic proximal colon. The appendix was not visualized. Doctor Kantor's findings were identical with mine.

Cholecystography failed to visualize the gall bladder. No shadows of either hard or soft stones were seen.

Gastric analysis revealed normal acid figures.

Feces were negative for ova and parasites. Lamblia, encysted or free, were not detected.

At this stage of the study, a *diagnosis of cholelithiasis* was based upon (1) the clinical history, (2) secondary evidence of gall-tract disease (persistent drawing in of the duodenal bulb) and (3) direct evidence in the non-visualization of the gall bladder roentgenologically.

Diagnostic biliary drainage showed no cellular evidence suggestive of gall bladder pathology but the syphonates contained numerous actively motile flagellate protozoa in strands of mucus, identified as *Lamblia intestinalis*. No definite sequence of biliary fractions was obtained in the first biliary drainage. Two days later drainage was again resorted to. The macro-microscopic findings were essentially as in the first drainage with *Lambliae swarming* each field of study. These findings were confirmed by Doctor J. L. Kantor.

It was our impression that the reason for failure of gall bladder visualization on five occasions at that time, May 1931, might be ascribed to the cystic-duct catarrh brought about by the *Lambliasis*. Fat globules were seen in aspirates in response to $MgSO_4$ instillation. The protozoa probably had ascended via the common duct, to the gall bladder. Biliary drainage thus proved its value, diagnostically, by revealing *Lamblia* infestation in an instance which otherwise would have been labeled cholelithiasis.

Differential leucocyte count revealed no eosinophilia.

Therapeutically, arsphenamine seemed to be indicated, since it has been claimed that the drug has a specific action against *Lamblia;* also because it improves the general condition. The first injection of 0.3 Gm. neoarsphenamine was given without toxic reaction. Several days afterward biliary drainage disclosed no parasites. The patient appeared much improved and free from symptoms. The second injection, 0.6 Gm. of the drug, was given with no immediate toxic reaction. On the third day following the second injection, the patient's attending physician, Dr. Ben Arbor, New York, reported that within 72 hours following the injection "the patient developed a generalized maculo-papular eruption which appeared first on the face and then spread to the rest of the body. Associated with it were edema of the face, intense headache and dizziness; temperature 101° by mouth. The itching was intense, relieved to a degree by the usual treatment. A urinalysis done on the first day of the eruption exhibited a trace of albumin. The same day sodium thiosulphate was administered with some improvement of symptoms. This was repeated for the two days following with disappearance of rash and other symptoms."

February 15, 1932. Patient had an attack of epigastric distress, which lasted for a few hours and developed into a clinical picture of biliary colic. However, it responded to simple treatment.

July, 1932. Patient looked well, had gained weight, and had no dyspeptic attacks. Cholecystography at this time failed to visualize the gall bladder.

February 23, 1933. Patient still gaining weight, was almost symptom-free; however, she was conscious of "something" in the right upper quadrant. Biliary drainage was not successful; fluoroscopy showed the tube looped and its distal end to the left side of the spinal column.

March 27, 1933. Patient given 1/100 grain of atropine sulphate subcutaneously and intubated. Fasting residuum revealed nothing abnormal. "A," "B" and "C" bile fractions were obtained at this session. The aspirated floccules on microscopic search revealed no *Lambliae* or cellular evidence of chronic cholecystitis. The amount of "B" bile aspirated was 28 c.c. No "B" bile was recovered in response to $MgSO_4$ instillations. Occult blood was found positive in several specimens.

Note: The negative microscopic findings for either *Lamblia* or cholecystitis and deficient amount of "B" bile aspirated offer suggestive evidence that the capacity of the gallbladder had become lessened, possibly because of a thickened gallbladder wall.

March 30, 1933. Cholecystography failed to visualize the gallbladder.

April 3, 1933. Cholecystography repeated. Dr. J. C. Howard reported: "No radiographic evidence of calculus was observed. In view of the persistent non-visualization of the gallbladder at this and previous examinations, it is suggested that this is a chronic pathological gallbladder."

At the present time the patient relatively is free from symptoms, but experiences a sense of "weight and annoyance" under the right subcostal arch.

DISCUSSION OF CASE 1. This patient was referred to me to confirm a diagnosis of gall-tract disease. The outstanding clinical features supported by radiographic studies supported the clinical opinion. A routine biliary drainage disclosed *Lambliae.*

The following are pertinent questions:

Does non-visualization of the gallbladder imply primary pathology of the gallbladder, complete atrophy of this viscus, congenital absence, or failure of the dye for some reason to enter the gallbladder?

Can the symptomatology of cholelithiasis be ascribed to *Lambliasis*, or is the protozoic infestation a concomitant occurrence with calculi?

What damage is done by the *Lamblia?*

Briefly, the conditions which prevent dye excretion or exclude the dye-laden bile from the gallbladder are diseases of the liver and occlusion of the intra-hepatic duct system, the cystic or common ducts. Non-visualization from obstructive causes, except for cystic duct occlusion, are for want of evidence precluded from our discussion. Any disease of the liver would necessarily be very extensive to cause failure of dye excretion.

Opposed to such explanation in our patient are the mode of onset of symptoms and the duration for three years without frank icterus due to common duct obstruction.

Kinking of the cystic duct lacks operative confirmation, as also does the rare anomaly, congenital absence of the gallbladder. With respect to the latter, attention is called to the fact that at biliary drainage normal bile fraction sequences were obtained.

Non-visualization of the gallbladder in subacute appendicitis has been reported. Roentgenologically, the appendix in the present case was not visualized; there had been no clinical evidences of appendix disease and on examination there was no appendix region tenderness. One may advance the opinion that cystic duct catarrh dependent upon actively motile *Lambliae* might have obstructed the cystic duct sufficiently to prevent dye entering, and thus visualization of the gallbladder. Such cystic duct obstruction, occurring at intervals, would account for colicky pains.

CASE 2.—Mrs. B. M., age 37, *multipara*, exhibited intense jaundice. Preceding the icterus, she had suffered three days from fever and generalized muscular pains.

Physical examination was negative except for generalized intense icterus of skin and mucosae. The stools were clay colored, and the urine was very dark.

The urine was slightly positive for urobilinogen in 1 to 20 dilution. The icteric index was 100. The Van den Bergh test on May 26 gave an immediate direct reaction.

Two routine attempts at biliary drainage, at three-day interval, failed although fluoroscope showed that the tube was in proper position.

Following a subcutaneous injection of atropine sulphate, grain 1/100, light colored bile with fine flocculation later was obtained by the gravity duodenal tube syphonage. On microscopic examination this material revealed immense bile globules in association with mucus shreds. The appearance was similar to Lyon's description of aspirates in cystic duct catarrh—"an oleogenous material which melts out into globules, pools and lakes." This is due to the fatty ester of cholesterol. These droplets appeared as translucent, gray, neutral fat globules. They were unlike the brilliant chrome-yellow of healthy bile.

At this stage the icteric index was reduced from 100 to 75, the Van den Bergh reaction was changed from a direct immediate to a biphasic, and urobilinogen was positive in 1:30 dilution instead of 1:20.

A week later, microscopic examination of the bile aspirates, revealed actively motile protozoa identified as *Lambliae.* Neither parasites nor ova were found in the feces. The feces were brown in color and positive for urobilin. Differential leucocyte count disclosed no eosinophilia.

In about five weeks cysts of *Lamblia intestinalis* were found in the stools. The patient at this time was free of all symptoms; there was no trace of jaundice. On cholecystography (Graham method) there was very faint visualization of the gallbladder with evidence of pericholecystic adhesions.

COMMENT ON CASE 2. The salient features were:

(1) Clinical jaundice, (2) *characteristic behavior of the*

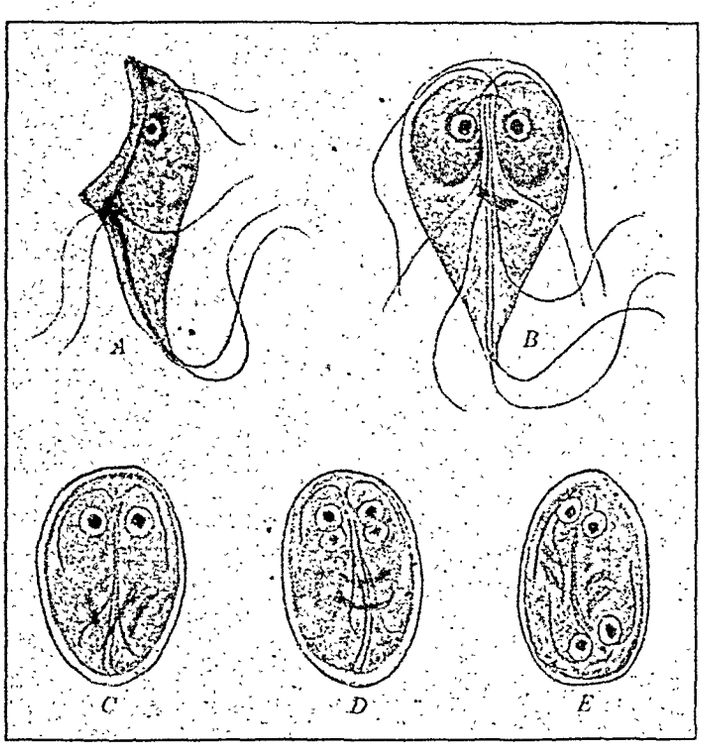
Van den Bergh reaction from direct to biphasic and to indirect as the icterus receded, (3) presence of *Lamblia intestinalis* in the biliary aspirate on two occasions, (4) characteristic microscopic picture of oleogenous droplets in biliary aspirate (cystic duct catarrh) and (5) presence of *Lambliae* in the feces.

Because of the jaundice, neo-arsphenamine injection was contraindicated. Even when the jaundice disappeared, it was felt that arsenicals still were contraindicated because of the possibility of residual perenchymatous hepatitis. Also because of this reason the Graham test was resorted to only after all traces of jaundice had vanished.

The only treatment which proved efficacious was biliary drainage for three hours at each period followed by transduodenal lavage with 240 c.c. of normal salt solution. There was a quick, favorable, clinical response to this therapy supplemented by bed-rest, diet and symptomatic management.

GENERAL DISCUSSION OF LAMBLIASIS PARTICULARLY OF THE BILIARY TRACT, AND RESUME OF LITERATURE.

Nomenclature. This flagellate was first known as *Lamblia intestinalis* in honor of Lamble, later *Giardia intestinalis*.



Giardia intestinalis. (*Lamblia*).

A and *B*, trophozoites as seen from lateral and anterior view. *C*, *D* and *E*, cysts in different stages of development. Drawings of specimen stained by iron-haematoxylon. x 2000. (*Lynch*).

Morphology. Living *Giardia* is a pear-shaped or tennis-racket shaped flagellate protozoan with a cuplike depression or "hold fast" near the anterior extremity by which it attaches itself to the intestinal mucosa. It has eight flagella, arranged in pairs, three at the edge of the cuplike depression, one pair at the posterior extremity of the parasite. In the biliary syphonates they are found in the strands of mucus. They are not bile stained. As Smithies stated years ago, the writer emphasizes that $MgSO_4$ is the ideal stimulant for diagnostic biliary "drainage" when parasites are suspected in the upper small bowel. Magnesium sulphate may cause detachment of the parasite from the mucosa, and enables its easy recognition in aspirated material.

The motility of *Lamiblia* may be compared to that of spermatazoa examined when freshly obtained and studied on a warm stage. Stool recognition is difficult unless the feces are fluid and examined promptly on a warm stage or hanging-drop preparation. Zahorsky[1] stresses the uselessness of sending the stool to the laboratory as a delay of only half an hour may result in loss of motility.

On the other hand the tenacity of the parasite may be appreciated by the fact that, although our patient used catharsis from the inception of her symptoms, the parasite thrived in its natural habitat unaffected by purgation. McCrae, in Osler's Tenth Edition, states that the *Lamblia intestinalis* was a frequent cause of enteritis during the recent war. *Lambliae* have been found in sputa in cases of gangrene of the lungs and of bronchial stasis and in the exudate of pleurisy. Their mode of migration from their duodenal or jejunal *habitat* is convincing evidence of their ability to travel from distant foci.

Habitat. The duodenum and jejunum. Paulson and Andrews[2] state: "*Lamblia* is the only protozoan inhabiting the duodenum and possibly the jejunum in human adults presenting protozoa in discharged specimens of feces but manifesting no clinical evidence of organic disease."

A study was made by these writers to determine the types and number of protozoa living in the duodenum, and possibly in the gallbladder and biliary system, by examination of the duodenal aspirates from human adults free from organic gastro-intestinal and hepatobiliary disease and presenting cysts or trophozoite forms of protozoa in discharged specimens of feces. Of 17 adult cases studied "11 showed single and 6 presented mixed infections of protozoa in defecated specimens of feces." It was noted that no organism was encountered in duodenal aspirates save Giardia *Lamblia*. The writers emphasized that in some of the defecated specimens other protozoa were found in addition to *Lamblia*, yet the drainage fractions revealed only *Lamblia*.

Geographical Incidence. Geographically, formerly it was thought that *Lamblia* was limited to tropical and subtropical climates, but a survey of the literature discloses more occurrence of this infestation sporadically in patients who have not resided in tropical or subtropical countries than was expected. I am in accord with Lyon, who says :"The recognition of *Lamblia* has come chiefly from the finding of the encysted parasite in the stools and there has been a very distinct failure routinely to seek for its presence in its actively motile state in the duodenum. Its evidence may become larger if we extend our routine examinations of the duodenum to include a search for it." In eleven cases from which Lyon recovered living *Lambliae* only one of the patients had ever been in a tropical or semi-tropical climate. The single case of Kantor, the nine cases of Hollander (170 patients routinely examined), and the one under discussion all occurred in residents of New York City.

Mode of Infection. Human *Lambliasis* is spread by the ingestion of the cysts of the *Lambliae* derived from the feces. Man may ingest the cysts directly by contamination with feces on his fingers, food or water, or indirectly through the agency of the house fly, which may feed on excreta containing the cysts and then deposit them apparently uninjured in its dejecta on food, particularly raw garden-truck, or drinking water.

Eosinophilia. This is not a constant finding. Peterman[3] reported two cases in children in which no eosinophilia were found. Simon[4] noted in a study of eight cases in which *Lambliae* were found in the course of routine examination of the stools that the blood findings showed "an absence of distinctive features." In one case, a six percent eosinophilia was observed, but this was caused by a coincident *trichuriasis*. Lyon and Swalm[5] state: "Absence of noteworthy eosinophilia therefore seems to distinguish this infection from other forms of parasitism." In both of my cases eosinophilia was absent.

Prevalence of Diarrhea. In the patients here reported one could not point to either diarrhea or constipation. The first patient exhibited chronic constipation; the second made no complaint regarding bowel actions. However, reports seem to vary, depending apparently on the zone of the occurrence

of the *Lamblia infestation*. Thus Smithies[6] reports that diarrhea and constipation were conspicuously absent in his cases.

Hollander[7] asserts that in three of his cases there was no diarrhea and constipation was a dominant feature. From a statistical point of view, Boeck[8] rationally concludes that "there is little evidence to support the view that *Giardia* causes diarrhea." McClendon[9] calls attention to the fact that whereas *diarrhea is one of the most frequent symptoms* associated with intestinal infections, it was encountered only once in a series of 22 cases of *Lamblia* infection, in marked contrast to the fact that constipation occurred in 50 per cent of the patients. "Blood," writes Simon,[4] "apparently does not form a characteristic feature of *Giardia* stools, a point which might prove of clinical value in the differentiation from the diarrhea of endamebic origin." Zahorsky and McLoon[10] record a series of children and conclude that *Lambliasis* has a definite place in the etiology of the diarrheas in children; they feel that the parasites produce a distinct irritation of the intestinal tract in children which irritation and diarrhoea may result in malnutrition and secondary intestinal infestation.

There seems to be a sort of commensalism between *Lamblia* and *endameba histolytica*. Carr and Chandler[11] cite a soldier who presented himself as a diagnosed case of duodenal ulcer, but the conclusions drawn from physical and roentgen examinations were that a gastric or duodenal lesion did not exist and that the irritable intestinal tract was due to a parasitic or reflex cause. Microscopic examinations of the stools revealed a few motile forms of *endameba histolytica* and numerous cysts of *Lamblia intestinalis* of the so-called "large race" were found.

Pathogenicity. Hollander[7] draws attention to the fact that the earlier writers believed *Lamblia* non-pathogenic. "Since the Great War," he states, "most authorities hold that while no symptoms are exhibited when the flagellates are few in number, they amy become pathogenic when they are present in enormous numbers; then they cause an enteritis and diarrhea of moderate severity. . . It was emphasized that each of these cysts was derived from a flagellate organism provided with a 'sucking disk' whereby it abstracted its nourishment from the intestinal epithelial cells." Hollander further states that Fantham and Porter found that intestinal lesions could be produced in kittens and mice by the suctorial action of the flagellates.

The reason some authors consider *Lamblia duodenalis* as non-pathogenic is because the protozoan may be found in healthy individuals, especially in the tropics. Following a saline purge *Lamblia* was found in the stools of more than 25 percent of apparently healthy persons.

Pathogenicity, then, is apparently a moot question. But we are of the opinion that, until we know more about this parasite, it would be unwise to consider it non-pathogenic. The attachment of the flagellate to the epithelium of the duodenal mucosa constitutes pathogenicity in itself. This close cellular relationship would appear to be detrimental to normal cell environment and therefore may be pathogenic. Zahorsky and McLoon[10] sum up their study thus: "*Lambliasis* has a definite clinical importance, since the protozoan in infants and young children produces a distinct irritation of the intestinal tract which may result in malnutrition and secondary intestinal infections."

In the literature, the following conflicting opinions are held as to the pathogenicity of *Lamblia:* (1) always pathogenic, (2) pathogenic through prolonging an already existing condition, and (3) a harmless commensal. The writer accedes to the first two views, but the type of symbiosis manifested by a harmless commensal is far from his understanding.

C. G. Lucas[12] asserts: "While I know that some men believe that *Lamblia* is not pathogenic, still some of the worst cases of intestinal parasites, three at least, have been caused by *Lamblia*." He relates of one man who searched for relief from the Atlantic to the Pacific, and became *sans* teeth, *sans* gallbladder, *sans* appendix, "and only at Johns Hopkins Hospital, where he was given mercurochrome through a tube, did he get any relief." Surely in cases where anatomical pathology cannot be established, this "commensal" association may be regarded as clinically pathogenic.

When the clinical behavior is stormy, hasty surgery may be exhibited in the absence of microscopic scrutiny of the biliary aspirates. Such procedure adds insult to a type of existing clinical pathology which is best treated by non-surgical drainage. Carr and Chandler[11] draw attention to the fact that "*Lamblia inteslinalis* is now fairly definitely established as a pathogenic protozoan. In fact this flagellate recently has been described as the causative organism of 'trench diarrhea' a dysenteric affection which a number of overseas troops experienced and from which some returned soldiers still are invalided." It may not be an error to call, clinically, *Lamblia infestation* "trench diarrhoea" regarding the ailment as due to faulty hygienic environment, wherever it occurs, not necessarily in trenches: as the term "trench mouth" is applied to Vincent's infection, inasmuch as both conditions occur in civilian life.

Lyon[13] refers to the postmortem findings present in 187 cases of pure *Lambliasis* studied by Fantham and Porter.[14] They report "that erosion and distortion of the intestinal epithelial cells had occurred owing to the direct suctorial action of the flagellate." Such findings justify, it would appear, the theory that *Lamblia* may be responsible for actual pathology.

In infected mice, postmortem studies made by Fantham and Porter lend direct support to the view that these flagellates may cause tissue damage. The histopathologic findings were: erosions of the mucous membrane, small duodenal ulcers, and desquamated epithelia to which are attached *Lambliae*, evidences of an inflammatory process. All mice were infected with *Lambliae* from man. Opinion nevertheless is sharply divided over this question of pathogenicity; the organism is considered non-pathogenic by many advocates as shown in an extensive literature.

The first American instance was reported by Hemmeter in 1902, after a lapse of 43 years since Lamble (1850) discovered the flagellate. A survey of the literature conveys the impression of a concerted opinion that *Lamblia* may be a contributing factor to disease or dysfunction particularly involving the gall-tract, the duodenum, and jejunum. It is not known why this parasite selects as its chief abode the upper small bowels. By its peculiar oral sucker it attaches itself to the duodenal epithelium and may penetrate within the deeper glandular layers. It is readily recognizable by microscopic examination of fresh biliary aspirates. The flagellates, by themselves, may be not pathogenic in the sense of organisms which produce toxins, but by their presence may irritate the duodenal mucosa and cause inflammation in the periampullary region. Edema results; duct obstruction and icterus may follow. Examination of a fresh biliary aspirate may reveal that *Lamblia* are swarming in the duodenum in countless numbers. Since they are actively motile, should they invade the biliary ducts clinically, obstructive symptoms simulating cholelithiasis may arise.

So abundant may the parasites be in duodenal aspirates, and so resistant are they to therapeutic measures, that one finds it difficult to be convinced that they may not cause or aggravate existing lesions. Simon,[15] New Orleans, states: "It is thinkable that a toxin might be secreted by the organism and that mechanical irritation to the intestinal mucosa may be present which may produce a very mild degree of irritation and pathogenicity."

Lynch,[16] on the other hand, denies pathogenicity "Thus far, considering the intestinal flagellates as a group, I have been unable to incriminate them of pathogenic activity. . . . The results of the study, thus far obtained, seem to lend little or no support to the growing tendency to incriminate intestinal flagellates as pathogenic agents, but rather to the contrary."

McGill[17] in line with Lynch writes: "*Lamblia intestinalis* was long considered a nonpathogenic inhabitant of the bowel. Even recently Kofoid, Konhauser and Plate found this flagellate in 6 percent of 1500 healthy American soldiers." Yet later he qualifies his opinion thus: "many clinical observations in the last ten years have established *Lamblia* as the probable cause of some severe chronic diarrheas." She relates that "one man in robust health had occasional attacks of pain above the umbilicus and diarrhoea, with from thirty to forty stools a day, containing many organisms; there was an eosinophilia of 10 percent. One woman, aged 50, had a severe diarrhea of three months' duration rebellious to all treatment, with enormous numbers of *Lambliae* in the stools, and an eosinophilia of 8 percent. She died from progressive debility; her brother had died several months before from a similar condition." Kantor[19] remarks: "the most common clinical condition associated with *Lamblia* infection is an enterocolitis." He mentions the tendency of the organism to invade the bile passages and the gallbladder and quotes Smithies' report of the actual presence of *Lamblia* an infected gallbladder removed at operation. There is a convincing mass of evidence supporting the view that a parasite with the structure and attributes of *Lamblia* has all the attributes of pathogenicity.

Mimicry of disease with special emphasis to gall-tract disease. The outstanding symptomatology in the cases under discussion suggests disease involving the biliary apparatus. Since the protozoan dwells in the upper small bowel, its presence in the gallbladder speaks strongly for an ascending infestation of the gall duct system, particularly when one recalls the active motility of *Lamblia*. It is conceivable that highly motile "large race" organisms may carry pathogenic microorganisms with them from the bowel into the biliary duct system; in such instance *Lamblia* serves as a "carrier."

In our case the symptomatology suggesting a surgical condition after the protozoa apparently had been destroyed by arsenical therapy, and the persistent non-visualization of the gallbladder roentgenologically, suggest permanent pathology prior to the death of the flagellates.

Boeck[8] divides the clinical manifestations which have been attributed to *Lamblia* in man into three groups: "(1) diarrhea, persistent or intermittent with intervals of constipation; (2) chronic gallbladder disease with symptoms of epigastric or right upper quadrant pain, discomfort or tenderness, dyspepsia; (3) certain other obscure conditions in which the etiology is not present."

He refers to a case (reported by Fairise and Jannin) of severe diarrhoea for ten months with *Lamblia* found in the stools. The possibility of intestinal tuberculosis, bacillary and amebic dysentery and worm infestation was ruled out. The case came to necropsy; a large mammelonated, cauliflower-like growth with ulcerations was found in the cecum, and ulcers were present in the transverse colon and the lower ileum; the remainder of the small intestine was negative. Microscopic examination of fixed and stained tissues revealed ulcers with necrotic purulent edges filled with cellular debris. Marked leucocytic infiltration was present, and both motile and encysted forms of *Lamblia* were found in the mucosa, submucosa and in the muscularis whenever an ulcer extended so deeply. Boeck comments and questions: "This evidence is the strongest of any known that tends to incriminate *Lamblia* as a true pathogenic parasite of man, but unfortunately the case is obviously not crystal clear. The condition of the duodenum and jejunum, the regular habitat of *Lamblia*, was reported as normal, while the flagellates were found in gross lesions outside their normal abode, i.e. the lower ileum, cecum and transverse colon." This case presents basic reasons for a protracted diarrhoea even in the absence of *Lamblia*. But concomitancy of maladies is not an uncommon occurrence, and it is therefore plausible to assume that colonic hyperperistalsis engendered by the aforementioned basic etiology sufficed to bring down the protozoa from the upper small bowel to be imbedded in the ulcers and interstices of the neoplastic tissue where some of them underwent encystment. Finally, Boeck qualifies opinions regarding pathogenicity by stating ". . . at any rate, *Lamblia intestinalis* may produce sufficient irritation of the small intestine to justify us in regarding it as pathogenic. But, to date, I know of no pathologic evidence gained from a study of stained sections of the intestine that lends any proof to this idea, and clinical evidence alone is not sufficient. . ."

The writer's Case 2 was subjected to cholecystography eight times after the inception of the attacks of biliary colic but the gallbladder never was visualized. This fact indicates the presence of a lesion of this organ, the true nature of which may be discovered at operation. But, since the case at the present writing is entirely silent clinically, it is unlikely that a pathologic study of the gallbladder soon will be possible. With us, the question whether or no *Lambliae* invade the gallbladder has not been answered. However, Smithies[6] reported the presence of *Lamblia* in two gallbladders removed at operation.

Lyon refers to Silverman's statement: "We found the same character of bile as was recovered by the duodenal route, but while the latter contained myriads of *Lambliae*, neither did the gallbladder mucosa nor its contents reveal any of the parasites or their cysts." In Lyon's own case, "no *Lambliae* were found either in gallbladder bile or scrapings from the mucus membrane of the gallbladder containing 155 stones, but there is considerable clinical evidence that infestation of the gallbladder or ducts is a possibility."

It occurs to us that cholecystitis without calculi, the result of an ascending infection, may be brought about by these highly motile trophozoites, which may carry pathogenic organisms to neighboring regions. But this is not probable in calculous cholecystitis because of the time factor involved in the genesis of stones. The *Lamblia*, if coexistent, would have manifested its presence long before stone formation in the gallbladder took place. The findings of viable *Lambliae* in the gallbladder following its removal has been reported only in the two cases of Smithies. In our case the "A" fraction bile syphonate was the one which swarmed with *Lamblia*, especially in response to $MgSO_4$ instillation, but no characteristic "B" bile was obtained, and what looked somewhat darker did not contain the flagellates. We feel justified in concluding that *Lamblia* and gallbladder disease may be concomitant in the non-calculous gallbladder. The symptomatology might be ascribed to gallbladder dysfunction, *Lamblia* only supplying the irritant, or serving as "carriers" of bacteria. Destruction of the protozoan does not imply cure of gall duct or gallbladder pathology. In this respect the writer supports Kantor[18], who maintains that "elimination of the primary *Lamblia* infection is by no means synonymous with cure, or at least with the immediate cure of associated cholecystitis." Our cases demonstrate a clinical amelioration, but persisting gallbladder malfunction or duct obstruction is evidenced by repeated failures to visualize the gallbladder roentgenographically.

Maladies which have somewhat similar symptomatology are duodenal ulcer and gall-tract disease. Because of the association of a post-pyloric ulcer and biliary tract disease, or the likelihood of a duodenitis, mimicry exists between gallbladder malfunction and a duodenal lesion. All of these factors divert attention from *Lambliasis*. Ordinarily the parasite is not even suspected, much less looked for.

A striking instance of a wrong differential diagnosis in gastro-enteric disturbances is demonstrated in the case reported by Stevenson[19]. His patient was examined thoroughly, but a stool examination was not made. At a later date, in a neighboring city, the patient's stool was examined and found loaded with *Lambliae*. In another case, subjected to removal of tonsils and hemorrhoids, the feces were found to be infected with *Lamblia* and there followed a temporary amelioration of symptoms. They returned and cholecystectomy and appendicectomy were performed. The patient returned "with the same train of symptoms, although minus a gall-

bladder. On examination it was found that he still had intestinal parasites which, in my opinion, (Stevenson) were the source of the trouble all the time, and had simulated gallbladder disease closely enough to cause the removal of the organ."

Stevenson cites another example of apparent concomitancy. A widow, aged 45, gave a history pointing to gallbladder attacks. These had occurred over a period of several years at periodical intervals. *Lamblia* was detected, and the condition was treated without symptomatic relief. A roentgenologic investigation revealed a gastric ulcer which yielded to therapy.

TREATMENT

In our first case, treatment was interrupted by a marked arsenical reaction. The patient had in all six biliary drainages with transduodenal flushings at the termination of the procedure.

Flagellates were detected in the first two intubations only. A survey of the literature convinces us that attempts at eradication of *Lamblia infestation,* once it has firmly entrenched itself in its natural habitat, are not attended with success. The flagellates are very resistant to drugs. All sorts of so-called intestinal disinfectants have been employed without effect upon the organisms. Ipecac and emetin were found devoid of influence over this type of intestinal protozoa. Arsphenamine gave good results. Simon[4] used arsphenamine in six cases. In one case, that of a five-year-old girl, the drug was introduced directly into the intestinal tract through the duodenal tube; in the others, it was given intravenously. All showed prompt disappearance of the cysts from the stools. Subsequent investigation failed to disclose further traces of the infection.

RESUME OF THERAPEUTIC AGENTS SUGGESTED

A—Bismuth salicylate in the treatment of children.

B—Stovarsol (acetarsone), three doses daily for seven days, repeating at weekly intervals. Stevenson[19] believes that in certain cases stovarsol is of benefit in addition to neo-arsphenamine.

C—Controlled doses of *thymol* followed by a saline (Smithies[6]) with transduodenal lavage with $MgSO_4$ solution, at temperature of 110° F. (following de Riva's studies upon the thermal death points of protozoa) and spaced, intravenous injections of salvarsan. Several "courses" of such therapy are followed during three months time. When thymol is not well-borne calomel (dose 5 to 10 grains) is exhibited at intervals over several months. Duodenal aspirations are employed freely. Smithies controls thymol exhibition as follows: Put the patient upon the fat-free diet for 3 days; empty the alimentary tract with $MgSO_4$; administer thymol from 40 to 80 grains in enteric capsules at two-hour interval—two doses at each "course." After six hours the bowel is emptied by saline.

D—Arsphenamine instillation directly into the duodenum through the tube. This method proved to be only partially successful (Simon[4]). Administration of arsphenamine by rectum where the intravenous method is refused, or where the veins are so small as to cause unusual difficulty through the intravenous route. Neo-arsphenamine intravenously in small doses at weekly intervals until three or four doses are given. This method is the one of our choice.

From a clinical standpoint, the patient may remain free from parasites, but if damage already has been done to the gallbladder or ducts, may be conscious of right upper quadrant discomfort. This fact, together with non-visualization of the gallbladder roentgenologically, is an indication for surgical intervention. However, the patient often interprets the subsidence of the severe symptoms or disappearance of icterus as a cure and declines operation. If our case ever comes to operation, some of the premises in this paper will be clarified. The results will be recorded.

SUMMARY

1. Two cases of *Lambliasis* associated with cholecystitis and simulating cholelithiasis are reported. In one case the infestation responded to neo-arsphenamine but treatment was followed by a severe arsenical dermatitis which was successfully combated with sodium thiosulphate.

2. There appears to be no specific symptomatology of *Lamblia* infestation other than mimicry. The diseases which *Lambliasis* simulates are affections of the gallbladder, duodenal ulcer and colitis, with or without diarrhoea.

3. An instance of catarrhal jaundice is reported with detection of *Lamblia* in the stools and biliary aspirates. It responded favorably to treatment.

4. Combined routine stool examination and microscopy of the biliary aspirates should be made in all gastro-intestinal conditions.

5. *Lamblia* is prevalent in tropical and sub-tropical climates, but sufficient evidence has accumulated that the protozoon may be found in temperate zones.

6. The attachment of the flagellate to the epithelial cells in the duodenum and jejunum seems to be evidence of pathogenicity: directly at the site of attachment and indirectly to adjacent organs, as the biliary apparatus and remotely the colon.

7. The fact that the *Lamblia* is not bile stained is evidence that its habitat primarily is in the duodenum unless the parasite is a chromophobe.

8. The multiplicity of the therapeutic agents offered for eradication of *Lamblia* is indication of the marked resistance of this parasite.

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BRILLIANT BLUE FCF
A NEW DYE FOR DIAGNOSTIC GASTRO-INTESTINAL STUDIES*

A PRELIMINARY REPORT

By

ARTHUR C. TAYLOR, M.D.
MADISON, WISCONSIN

FOR purposes of diagnosis of gastro-intestinal motility and of fistulae, lampblack and carmine frequently are employed. Lampblack is a fine solid and may be identified only with difficulty. The red stain produced by carmine also presents difficulties of demarcation. Neither is entirely satisfactory in a study of patency of suspected fistulae. Methylene blue, besides being subject to fading in color, occasionally gives rise to reactions of irritation in the gastro-intestinal tract.

At the suggestion of Professor A. L. Tatum, we undertook a study of the use of a blue pigment, "Brilliant Blue FCF."† This pigment has intense color potency, low toxicity, and furnishes quite unequivocal differentiation because of the sharp demarcation between its blue or blue-green staining, and either the yellow fecal or red tissue color.

Dr. Tatum's brief resume of the hitherto unpublished pharmacological study of Brilliant Blue FCF is given below:

DATA REGARDING BLUE FCF

The maximal tolerated dose of Brilliant Blue FCF, administered in watery solution orally, is, for rabbits, 2.5 to 6 grams per kilogram, and for dogs, more than 1 gram per kilogram. When given to dogs in solid form in gelatine capsules, the material may cause what appears to be gastric irritation with resulting emesis. In man, doses up to 0.5 gram, either in capsule or in solution, produce no gastric symptoms; but if over 0.5 gram be given, diarrhea is likely to occur. Given orally to man, in entirely innocuous doses (0.25 to 0.45 gram per dose), the feces become intensely blue or blue-green in color with a sharp line of demarcation between stained and unstained portions. No trace of absorption occurs with these doses, as indicated by complete absence of abnormal color in the urine. In early toxic doses, the urine becomes greenish in color. Diarrhea appears to be the first sign of over-dosage when the material is administered orally.

CLINICAL EXPERIENCES

Brilliant Blue FCF was administered to a score or more of patients with a variety of disease conditions. In no case was there any gastro-intestinal or general toxic reaction, although the dose of dye ranged from 300 mgm. to 500 mgm. If much larger doses were given, a slight diarrhea resulted. When the dye appeared in the formed stool, the line of demarcation was very sharp and the disappearance from the stool also was very definite though not quite so sharp. With this range of dosage there was no pigmentation of the urine by the dye, thus indicating absence of systemic absorption. The rate of travel through the intestinal tract varies with the individual or the disease, with a normal appearance in the stool in about 24 to 36 hours and a disappearance in about 48 to 72 hours.

Fecal fistulae from various sites along the gastro-intestinal tract show the passage of the dye. At the cecum, for example, the dye appeared in from 2 to 5 hours, while in the descending colon it appeared in from 6 to 9 hours.

In one patient with a high jejunal fistula, the dye appeared on the dressings in 5 minutes and was of a brilliant greenish-blue color. In another case of *suspected* fecal fistula from the cecum, the dye failed to appear. At operation, the sinus tract was found to extend to the outer surface of the bowel wall, but did not penetrate. The operation was simplified by this preoperative knowledge. In one case, Brilliant Blue FCF, when administered by mouth, failed to appear in a fistula from the sigmoid, the presence of which was proved by lipiodol injection. This failure is explained by the fact that the patient was extremely constipated and had had no bowel movement for the 48 hours prior to the administration of the dye, and when the dye did appear in the stool after 31 hours, the stool was extremely dry and constipated in character. It is believed that an enema or a liquid stool would have allowed the dye to appear through the fecal fistula in this case. In a similar case of fecal fistula following tuberculosis of the spine, the dye was administered in an enema; this came out through the fistulous opening promptly.

In another patient, lipiodol injections twice failed to show the sinus penetrating the bowel, but the administration of the dye, by mouth, gave definite evidence of color on the dressings thus proving a fecal fistulous tract. This patient also had an extremely irritable bowel but experienced no toxic symptoms from the administration of Brilliant Blue FCF *per os*. Another case, one of recto-vesical fistula, is of interest. The dye was administered by mouth and appeared in 8 hours in both the urine and the stool.

CONCLUSION

Brilliant Blue FCF is recommended as a new non-toxic coloring agent, for use by mouth or by enema, in the study of such conditions as gastro-intestinal motility and suspected fecal fistulae.

*Department of Surgery, University of Wisconsin Medical School, Madison, Wisconsin.
†A certified food color, made by the National Aniline and Chemical Company.
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THE OCCURRENCE OF A PERNICIOUS ANEMIA SYNDROME IN THE PRESENCE OF NORMAL GASTRIC ACIDITY

REPORT OF AN INSTANCE*

By

A. L. LEVIN, M.D.†
NEW ORLEANS, LOUISIANA

IN SPITE of the long-continued and, as yet, unrewarded search for the essential causative mechanism in pernicious anemia, medical science has succeeded in conferring the most striking practical benefit upon patients with this disease through the discovery of certain substances (liver, stomach, etc.) which, when administered in sufficient amounts, effect a normalizing change in the blood-picture and may maintain the blood indefinitely at a normal level.

The systems chiefly affected by the disease are the gastrointestinal, the nervous, and the hematopoietic, but it is frankly uncertain just where the pathogenesis begins. Unfortunately, too few of the very earliest cases have been studied, but it is known that spinal cord changes may, in exceptional instances, precede by months or even years, the appearance of anemia: thus, well-marked, subacute, combined degeneration of the spinal cord may be long present before the rather specific type of anemia is noted, and Woltman[1] has commented upon cases in which the first symptoms of any kind consisted of a sudden, fulminating transverse myelitis with "cord bladder." Again, sore mouth with glossitis may, as Riesman[2] has pointed out, serve as reliable *inaugural* symptoms, so that such patients, even in the absence of blood changes, may be classed at once as pernicious anemia, provided they show definite anacidity on gastric analysis. Hayden[3] has gone even a step further and laid down the criteria upon which the *earliest* diagnosis of pernicious anemia may be made, namely, achlorhydria and increased individual cell volume, even in the absence of anemia, glossitis or nervous system manifestations. By employing these conceptions, no doubt many earlier diagnoses could be made. But of course, heretofore, and for many years, achlorhydria has been the *sine qua non* of the diagnosis, and only recently, has the profession been partly prepared to accredit the diagnosis in instances where normal gastric acidity was found.

A year ago, before this association, the author described 25 cases of *achylia gastrica* with anemia of simple type and gastro-intestinal symptoms, 75 percent of whom, on treatment with liver, showed marked clinical improvement and a return of free HCl to normal or nearly normal. In the discussion, it was suggested that we probably had presented cases of very early pernicious anemia. Bloomfield and Polland[4] feel that it is worth while trying the effects of liver extract on cases of anacidity especially when other abnormalities are present, such as simple anemia, quite apart from pernicious anemia. It is, of course, thoroughly established that in pernicious anemia, the gastric anacidity never changes, and in fact, Bloomfield and Polland consider that even "unexplained" anacidity (occurring without disease in otherwise normal persons) equally is permanent.

The priority heretofore universally conceded to gastric anacidity in the syndrome, pernicious anemia, is now at some risk of being challenged, in view of the increasing reports of instances in which all criteria for the diagnosis of the disease were present with the exception of anacidity.

Samuel Fenwick's[5] well-known investigations of gastric atrophy, placed more stress on the peptic power than on the acid content of the gastric juice, so that it remained for Cahn and von Mehring,[11] 1886, definitely to demonstrate the absence of free HCl in instances of true pernicious anemia. In 1921, Samuel Levine and Ladd[6] reviewed 143 well documented cases of the disease and found persistent achlorhydria in all but 3, in 2 of which the diagnosis was somewhat in doubt. Bloomfield and Polland studied 31 cases of pernicious anemia, using the histamine method of gastric analysis, and found that all but 1 case had true anacidity. According to Cornell,[12] HCl was absent in 99 percent of the cases which came under his observation. Many other similar reports have appeared.

The finding of free HCl in any given case has heretofore caused one to question the validity of the diagnosis of "Addisonian," pernicious anemia. However, Bloomfield and Polland make the following statement: "It must be admitted that, occasionally, one encounters an instance of what appears to be true pernicious anemia with an apparently normal gastric secretion." Castle, from a study of 2 cases, admitted the same possibility. Barnett[7] has reported the study of a patient who, by all present criteria, must be classed as pernicious anemia, although the gastric acidity was normal and Castle's intrinsic factor was demonstrated in high concentration. L. S. P. Davidson and G. L. Gulland report cases in which there was adequate acid secretion and Goodhart mentions a patient who repeatedly showed free HCl, with typical pathological changes at autopsy. According to Pepper, Farley and other clinical authorities, a response to specific treatment (characteristic reticulocyte increase with the later rise in the red blood cell count and hemoglobin) is, in itself, sufficiently pathognomonic of true pernicious anemia. Perhaps not everyone will accept this therapeutic test.

The patient forming the subject of this paper, presented a faithful picture of pernicious anemia, but free HCl was present in normal *titre*. It is possible that, in this patient, and in the few others reported in the literature, the pathological process first attacked the nervous and hematopoietic systems, avoiding the stomach until last; so that one may expect a disappearance of the HCl eventually, when total atrophy of the gastric glands has supervened.

In support of this view, we wish to call attention to the case of pernicious anemia reported by us a year ago in which free hydrochloric acid to the value of 17 developed under liver therapy and remained for only three weeks; since then absolute achylia has been constant. This suggests that some of the gastric tubules were not yet completely atrophied when the pernicious anemia syndrome otherwise was fully developed. This observation may indicate that the first link in the pathogenetic chain of pernicious anemia does not always (or may never) include abnormalities of the gastric mucosa.

*From the Department of Medicine, Louisiana State University Medical Center.
†Professor of Clinical Medicine, Louisiana State University Medical Center.
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11. Cohn and von Mehring. Die Sauren des Gesunder und Kranken Lagen. *Deut. Arch. f. Klin. Med.* 39: 233, 1886.
12. Cornell, Beaumont S. *Sajous's Analytical Cyclopedia.* Vol. XV, p. 48.

HISTORY OF PATIENT

V. K., white, male, age 76. First came under my observation on April 23, 1933.

Chief complaint: Symptoms of indigestion, marked weakness, poor appetite, slight loss of weight, dyspnoea on the least exertion and vertigo on stooping. The patient stated that he felt so weak that he could hardly move his legs and that he often was disturbed at night on account of loose bowels.

Past history: Never operated upon. Was treated for typhoid fever by the Author about 22 years ago.

Present illness began in December, 1932 when first he experienced epigastric discomfort after a meal. About the same time, general weakness developed and his muscles became flabby and relaxed, his skin assumed a lemon color and his tongue became red and very sore; he became very dizzy on stooping. Looseness of bowels developed accompanied by numbness and tingling in the lower extremities. He vomited food only once during the course of his illness. The patient could not account for his marked weakness as he has been on full diet. For the past several months, the most distressing feature had been a burning sensation in the mouth and a recurrent sore tongue.

On physical examination the outstanding features were a definite lemon tinge and dryness of skin with pallor of the lips and gums; temperature was 100, pulse 78. The body appeared well nourished; reflexes in lower extremities were lost but there was no loss of sensation; pupillary reaction was normal; liver was enlarged and spleen slightly palpable; blood pressure was 126/80. There were no abnormal findings in the chest. The abdomen was scaphoid; no palpable sensitive areas or masses. No palpable adenopathy.

X-rays of the gastro-intestinal tract were negative for neoplasm or other organic lesion. Barium enema exhibited a normal colon.

Blood picture (April 24, 1933): Hemoglobin 39-45%; red cells 1,620,000, white cells 2,500, color index 1.48. S. Mon. 58, L. Mon. 1, neutrophils 11, moderate polychromatophilia, marked anisocytosis, macrocytes predominating. Blood study made at hospital (April 25) returned similar findings—"many macrocytes, reticulocytes 0.1%, fragility begins at .32 complete at .26."

Gastric analysis: Free HCl 50, T. A. 85, negative occult blood (April 24). Second gastric analysis: Free HCl 26, T. A. 60, negative occult blood (April 25).

Wassermann was negative. Icterus index was 32 (April 24). Van den Bergh: direct—delayed, indirect—weakly positive. The *urine* contained trace of albumin, *positive for urobilinogen*, negative for bile, few hyaline casts. Feces was negative for ova and parasites.

Proctoscopic examination revealed a pale mucosa but no ulceration.

Blood picture (May 2, 1933) (at hospital): Hemoglobin 55%, red cells 1,860,000, white cells 2,250, S. Mon. 55, Neutrophils 45, reticulocytes 1.8%, polychromatophilia, anisocytosis, macrocytes predominating.

TABLE I

Case of Pernicious Anemia with Normal Hydrochloric Acid

BLOOD PICTURES

Date	Hemoglobin	Red Cells	White Cells	Col. Ind.	S.M.	L.M.	N.	E.	Tr.	Reticulocytes
1933										
4/24	39-45%	1,620,000	2,500	1.48	58	1	41			0.1%
5/2	50-55%	1,860,000	2,250		55		45			1.8%
5/13	50-55%	2,920,000	6,000		23	1	61		5	4.3%
5/21	51-60%	3,180,000	9,250		17	5	75	2	1	4.5%
5/31	65-70%	3,860,000								5 %
6/6	67-70%	3,890,000								4.7%
6/27	74-80%	4,070,000	7,500		24	2	71	3		2 %
7/6	75-80%	4,080,000								1.8%
7/15	77-80%	4,210,000								1.5%
8/7	78-80%	4,280,000								1 %
8/15	77-80%	4,250,000								.8%
11/13	49-55%	2,610,000	2,500		44	1	55			4 %
12/12	55-60%	3,000,000								1.2%

Remarks: The blood pictures made on April 24, May 2, 13, 24 and November 13 showed polychromatophilia, anisocytosis and macrocytes predominating.
Patient was put on liver therapy on May 1, 1933. He discontinued the use of liver in August, 1933. Note prompt relapse (11/13/33 count).

POSSIBLE DIAGNOSES: Hemolytic jaundice; pernicious anemia; cancer of head of pancreas; sprue; intestinal parasites.

There was no evidence of sprue; the stool was not characteristic; there were no *monilia psilosis, taeniae* or other intestinal parasites. There was no X-ray evidence of malignancy; there had been no appreciable loss in weight. The blood did not show increased fragility; there was a superabundance of macrocytes and a diminution of reticulocytes. The indirect Van den Bergh Test was only slightly positive.

A diagnosis of *pernicious anemia* was made in spite of the normally acid gastric juice.

8. Bremer. *Fortschr. d. Neurol. Psychiat.* 1:12, 1931.

TABLE II

Gastric Analyses and Icterus Index

GASTRIC ANALYSES

Date	Bile	Free HCl	T.A.	Occult Blood	Enzymes	Icterus Index	
1933						1933	
4/24	none	50	85	negative	Positive— for rennin and pepsin	4/24	32
4/25	"	26	60	"	" " " "	6/8	16
5/13	"	27	50	"	" " " "	6/27	10
7/10	"	35	65	"	" " " "	8/7	16
11/15	"	75	95	"	" " " "	11/15	24
12/12	"	60	75	"	" " " "		

COURSE UNDER TREATMENT

The patient was put on liver therapy. His recovery was rapid. The reticulocytes rose to 5%; the red cells increased rapidly and the bowels became normal with, however, a slight tendency to constipation. Strength and appetite returned; the tongue improved although the patient complained on and off of a "burning" sensation of the tongue. He gained in weight. The blood count (August 15) exhibited: hemoglobin, 77-80%, red cells 4,250,000 and reticulocytes .8%. Icterus index dropped from 32 to 10. During this period the patient regularly was on liver medication.

Not realizing the importance of his continuing liver therapy, the patient became neglectful and eventually stopped taking liver. He reappeared on Nov. 13, 1933 with the same symptoms as before liver treatment was instituted. The hemoglobin was 49-55%; red cells 2,610,000; white cells 2,500; S. Mon. 44; L. Mon. 1; Neut. 55; reticulocytes 4%. As soon as liver therapy was resumed, immediately he began to improve. At the present writing, the patient is alive and remains comfortable when he follows instructions.

DISCUSSION

This patient presents all the characteristic features of pernicious anemia except the gastric achylia. The abolition of reflexes probably indicates an interception of the reflex arc in the postero-lateral columns of the cord, due to the degenerative process peculiar to pernicious anemia, although the vibratory sense had thus far been preserved.

The increasing number of reports of cases exhibiting free HCl in gastric extracts sooner or later will require the formation of new hypotheses regarding pernicious anemia etiology, although at present, the whole subject already is overburdened with theories. It is perhaps permissible to assume that achylia, like late cord changes and other phases of the disease, is the result of a gradual physiological decline.

How can we recognize pernicious anemia in its very earliest stages? Probably only by the most careful hematological and neurological examinations of persons showing achlorhydria, for this latter still must be our earliest lead. We are learning that substances effective for blood control (liver, stomach) have a much less specific and favorable effect on nervous system involvement; such agents seldom cause return of gastric secretion except in the case reported by the author in 1933.

The view of some clinicians that the cycle of pathologic events begins in the gastric mucosa is, of course, open to question. So far, the profession has failed to recognize many early instances of pernicious anemia with normal gastric secretion. Van Wart, years ago, went on record as believing that the cord changes, as indicated by the paresthesias, were frequently the earliest signs of the signs, although we know that this is not usually the case. Bremer[8] reviewing the central nervous system changes in pernicious anemia showed that neurological symptoms may at times precede all others and may, in fact, continue without blood changes, apparently indefinitely. The assertion that the neurological signs occur in 75 percent of the cases before other manifestations is allowable only if parasthesias be regarded as neurologic signs. Bremer does not subscribe to the assertion that achylia

gastrica is inevitable in pernicious anemia; few neurologists realized the importance of this finding until the work of Hurst and Bell indicated that achylia was just as constant in the subacute combined degeneration of the cord as in those cases showing specific blood changes. Piney was the first to report a "pure" case of cord disease with free HCl, and no doubt others will continue to follow. The studies of Ahrens[9] and of Young[10] both tend to encourage the recognition of neurological signs early in pernicious anemia. On the other hand, W. H. Riley, in a detailed clinical study of several hundred cases made by him with special reference to the involvement of the nervous system in pernicious anemia, the digestive disturbances and pathological changes also were carefully noted. Riley makes the following statement: "The digestive system was attacked first in nearly all cases as indicated by disturbances of digestion, achylia, attacks of diarrhea and other symptoms relating to the digestive tract." In the past several years a number of other investigators have called attention to the significance of intestinal symptoms in anemia.

9. Ahrens, R. S. *Arch. Neurol. and Psychiat.* 28:92, July, 1932.
10. Young, R. H. *J.A.M.A.*, 99: 612, Aug. 20, 1932.

The recent experimental work by Ephraim D. Boldyreff, with regard to the intestinal absorption of acids and its bearing on the causation of anemia, is worthy of notice. He concludes that absorption of acids from the intestine has a destructive effect upon the erythrocytes in the blood when there exists a deficiency in the alkaline secretion of pancreatic juice. The clinical study of cases of pernicious anemia reveals the prevalence of acidosis in this malady which is sometimes associated with high blood sugar.

In view of the divergence of opinion as to the early symptoms of pernicious anemia, an intensive study by clinicians should be undertaken to clarify the situation.

More careful evaluation and correlation of the total signs (hematological, gastric, neurological) in very early cases is the greatest present *desideratum* in our effort to formulate more comprehensive etiologic hypotheses. In these investigations, due attention to the presence or absence of the "intrinsic factor" of Castle is just as urgent as it is laborsome.

In the patient here reported, it is difficult to explain the presence of normal HCl unless on the basis of an unusual resistance of the gastric tissues in this particular individual.

ABSTRACTS

LEVY, JEROME S.

The Value of a Neutralization Test of Gastric Acidity in Patients with Duodenal Ulcers and So-called Pylorospasm. Ann. Int. Med., VII, 1218, April 1934.

Recognizing a double response on the part of the stomach to various types of test meals, Levy has attempted to determine the value of Elman's technic, which was developed to measure the rapidity and degree to which neutralization of the normally high acidity of freshly secreted gastric juices obtained in a given case. After reviewing some of the more important material in the literature dealing with that phase of gastric physiology bearing on the explanations of the neutralization of gastric acidity, he describes Elman's technic, which consists of aspiration of fasting contents from the stomach through a duodenal tube and the introduction of 300 c.c. of a 0.6 per cent hydrochloric acid solution. 20 c.c. of this were removed every twenty minutes until the stomach was empty. Titration of the specimens for free and total acidity were done in the usual manner. An Ewald test meal was also done on all but one of the series studied. Fractional removals were done every fifteen minutes, concluding the removal at the forty-five minute period.

The author's observations covered a series of 34 patients selected from a group of 60 consecutive patients admitted to the gastro-intestinal service of the Missouri Pacific Hospital, St. Louis. From this material data was compiled intended to show the results of a test for what he terms gastro-duodenal function. Inasmuch as the test solution was a counterpart of the normal secretion of the stomach, he argues that it is analogous to measuring the physiological ability of the gastro-duodenal team to neutralize the normal gastric juice. The results seem to show that patients with duodenal ulcer neutralize the test solution less rapidly and less completely than a normal stomach and that the emptying time was prolonged. Vagotonia contributed nearly identical findings; this group showed evidences of appendicitis and those operated on were relieved of the ulcer-like symptoms. Levy thinks the failure to keep the acidity down is not due to hyper-secretion, but rather to faulty neutralization. The author concludes that pure gastric juice is always secreted at the same level of acidity, hence the term hypo-neutralization to indicate high acid values is preferable to hyperacidity. By the same logic he would think in terms of hyperneutralization rather than low acidity or anacidity. Since Elman, Morton and Mann produced ulcers by drainage of the duodenal contents either into the lower bowel or to the outside, Levy thinks that high acidity is a significant factor in ulcer causations. Any mechanism that prevents reflux of duodenal juices into the stomach may thus be a contributing factor in high acidity; thus neuro-muscular irritability becoming a pylorospasm, duodenitis by impairing a reversion of peristalsis, or a decrease in neutralizing power of pancreatic juice, become features of moment. Since the secretory response of the stomach is markedly variable because dependent on so many subjective factors, and since the neutralization test depends on a single mechanism, Levy concludes it gives a more dependable estimate of the stomach function in a given case.

The reviewer of this article would emphasize (a) the thought that this is scarcely a diagnostic test, but rather a functional one; (b) that one would hesitate to agree that the collateral study with what the author refers to as the "ordinary Ewald test meal" is, in fact, a satisfactory Ewald test meal study. The bread is referred to as "two pieces," surely a rather indefinite unit of measure, and the water as "two glasses," likewise subject to some variation. It would seem that the same accuracy as described in the use of the acid solution might be desirable. The bread should be weighed and the water measured. Further, it is stated that three 15-minute fractional specimens were removed. A 45-minute specimen in many patients will not reveal the maximum acidity. (c) The gall bladder studies on the series were done with oral administration of the dye exclusively. It does happen that an intravenous dye study may show a normal gall bladder from an X-ray standpoint, after a failure to visualize or a poor visualization by the oral method.

Virgil E. Simpson.

BISHOP, EVERETT L.

Cancer of the Stomach in Young Patients. The American Journal of Cancer. April, 1934. (From the Steiner Cancer Clinic, Atlanta, Ga.)

The author calls attention to the fact that cancer in the young is frequently overlooked because of the age of the patient, and that this condition should always be considered in obscure gastric conditions.

Smithies and other authors are quoted in regard to subjective symptoms and objective findings, in order to show the atypical manifestations of this disease in the young; in a case reported by the author, a white girl sixteen years of age, showed no gastric symptoms, and the tumor was discovered only at autopsy.

Bishop states that the duration of the disease in the young may be figured in months rather than years, and in this opinion he differs from Dock. In most cases the onset is fairly sudden and the patient succumbs in a few months.

Smithies and Marble report cases having lived from three to five years. Pathology of the tumor, both gross and microscopic, is the same in the young as that found in old age.

The author calls attention to important findings; namely, the early and widespread metastases witnessed in most cases, the occurrence of metastases to the ovaries from the gastrointestinal tract, and the almost universal agreement that the "Krukenberg" tumor of the ovary is secondary to a tumor of the gastrointestiual tract, usually the stomach.

In Bishop's case, bilateral tumors of the ovary were noticed immediately upon opening the abdomen at autopsy, and the stomach was at once investigated. The tumor was invisible on its outer surface but was easily felt through the stomach wall.

The author presents a detailed and illuminating case report.

Ernest H. Gaither.

PORTER, ANNIE

Remarks on Intestinal Parasites in Montreal and Relation of "Endameba Histolytica to Colitis." (The Can. Med. Ass'n J., Feb., 1934, Vol. 30, No. 2).

These are the preliminary results of an investigation done at the Royal Victoria Hospital (Montreal) with a view to ascertain the "general incidence of animal parasites among patients" and to elucidate the etiology of colitis, a syndrome of frequent incidence in that city. The stools of 139 patients, male, female and infants, were examined soon after their admission. Patients suffering from intestinal malaise were chosen. The methods used were microscopical examination of fresh preparations in normal saline, methyl green, Gram's iodine, as well as a modified Willis-Barber salt flotation technique in each case. As many as 12 examinations of stools were done for one person, in certain cases.

Thirteen species of animal parasites were detected, including 5 species of Rhizopoda, 3 of Flagellata, 3 of Cestoda, and 2 of Nematoda. The endameba histolytica was found in 18 cases, the e. coli in 7 cases. Double infection occurred with 9 combinations of parasites, triple infections in 5 combinations.

So far, 29 cases of amebiasis have come under the author's notice. A few of those cases had "no suspicion of intestinal trouble, though they had suffered previously from diarrhoea." It must be pointed out these results are not representative of a population as a whole, being derived from a selection of patients studied at but one hospital in the city. Still, it would not be surprising to detect a larger number of such cases in a port like Montreal, where the population is cosmopolitan, seafaring, while the fruits and vegetables are imported from southern or tropical regions. This hypothesis would explain why a relatively high proportion of the patients studied were carrying amebiasis when they had never left Montreal. No direct connection with the cases contracted at the recent Chicago Exhibition was ever proven. These infestations "point to the need for proper sewage disposal, the keeping down of flies. . . and adequate prevention of contamination of water and vegetable foods by human excrement."

May we add that a study of quite a number of colitis cases with the same technique, excepting the Willis-Barber, is not yet showing the same results in some other hospitals of the City, although drugs like stovarsol bring a temporary improvement in the patients.

Jean R. A. LeSage.

HARDISTY, R. H. M.

Endameba Histolytica and Colitis in Montreal. (Can. Medical Ass'n Journal, Feb., 1934, Vol. 30, No. 2).

The high incidence of so-called "ulcerative colitis" in certain hospitals of Montreal have led the author to an extensive examination of the stools, in close association with Dr. Porter. Since March 1933, endameba histolytica has been observed in the stools of 21 patients (Royal Victoria Hospital). In most of the patients, symptoms were subacute, or absent. Four or five cases were residents of the City, and were registering their first attack. A woman of 52, also resident of the city died four days after her admission. In most of the cases the disease had lasted for several months or more. In one case a similar attack had occurred six years previously in Toronto. The two others were odd cases: the parasite being in the first instance detected in a case of advanced carcinoma of the sigmoid, the other, in a case of tuberculous enteritis Four patients had no dysenteric symptoms whatever, the endameba being discovered in the stools in routine examinations. These carriers constitute the greater danger to the community. "Most of the patients developed their symptoms in the City" says the author; others, very few, came from various countries; only one had stayed in a Hotel in Chicago in August, 1933.

Emetine hydrochloride was the drug chiefly used, given in small doses of one-half to one grain hypodermically once or twice daily for ten to twelve days. With this method the endameba disappears from the stools but seems apt to reappear within a few months. Carbarsone is apparently of a slower effect. Yatren enemata were used in one or two cases. The author gives his preference to emetine administered with caution, bearing in mind the possibility of toxic vomiting and diarrhea, and perhaps of circulatory depression.

In conclusion Dr. Hardisty suggests that a broader survey of the stools of patients admitted to the hospital be made, as the incidence of amebic infection is probably greater than believed, even in Eastern Canada.

We suggest that the methods for investigation of amebiasis be more standardized in the various hospitals of this country.

Jean R. A. LeSage.

ALTHAUSEN T. L. AND KERR, WM. J.

Hemochromatosis II. A report of three cases with endocrine disturbances and notes on a previously reported case. Discussion of etiology. Endocrinology. 17: 621-646, Nov.-Dec. 1933.

In discussing etiological considerations in hemochromatosis the authors mention excessive hemolysis, poisoning with copper, chronic alcoholism, and hepatic dysfunction. The conclusion is reached that two conditions are necessary to produce hemochromatosis: a constitutional predisposition of the liver or possibly some other organ, and a chronic intoxication affecting the susceptible organ. The most frequent toxic agent seems to be alcohol.

Instability of the blood sugar level is the cardinal feature of the diabetes in this disease. Resistance to insulin is rare and apparently develops as a terminal event. Cardiac failure due to hemosiderosis of the myocardium threatens to become a prominent lethal complication of hemochromatosis. Sexual hypoplasia occurs in about one-fifth of the cases and is probably due to deposition of hemosiderin in the anterior lobe of the pituitary. Treatment of the diabetes in the absence of fatal complications may be followed by diminution of cutaneous pigmentation and improvement in hepatic function.

Dwight Wilbur.

FRIEDENWALD, JULIUS AND MORRISON, SAMUEL.

Gastrointestinal Disturbances associated with the Endocrinopathies. Endocrinology, 17:393-413, July-August, 1933.

Friedenwald and Morrison emphasize that the endocrinopathies, particularly those of the thyroid, parathyroids, pituitary, and adrenals, play an important role in the production of digestive disturbances.

In considering the effect of the endocrines upon the gastrointestinal organs, three mechanisms must be considered: (1) Through the stimulation of control part of the vegetative nervous system; (2) by stimulation of the post ganglionic fibers and nerve plexuses of the organs themselves; (3) by direct action of the hormone on the receptive organs.

The effects of thyroid dysfunction are well recognized. Parathyroid defficiency is closely related to disturbances of calcium excretion and tetany is observed in gastroduodenal dilatation and upper intestinal obstruction. Disturbances of pituitary function give rise to obesity, enlargement of the abdominal organs, and to increased thirst associated with diabetes insipidus. In Addison's disease with cortical involvement marked gastrointestinal symptoms are produced. The effects on the gastrointestinal tract of some products obtained from these endocrine glands is discussed.

Dwight Wilbur.

BEAVER, D. C., HENTHORNE, J. C., AND MACY, J. W.

Abscesses of the liver caused by Bacteroides Funduliformis, Report of two cases—Arch. of Path. XVII, 493-509, April, 1934.

The several species of the Bacteroides comprise an interesting pleomorphic, non-sporulating group of organisms which, according to Bergey's Manual are obligate anaerobes. There are both gram negative and gram positive forms. The present authors believe that these organisms are deserving of a much more important place in an estimation of relative pathogenicity than they do now, in fact, occupy. The common sites of isolation have been the intestinal tract, and the genito-urinary tract, especially in the male, and they are also believed to be present in the throat and pharynx. The diseases that have been ascribed to this group of infectors are varied; they comprise many of the suppurative and gangrenous infections, such as appendicitis, male and female genito-urinary infections, pulmonary abscesses, empyema, otitis, cholecystitis, peritonitis, bacteremia, hepatic abscesses and multiple abscesses of liver, lungs, and spleen.

The present two instances of multiple hepatic abscesses were in men aged 61 and 50; the source of the infection was definitely colonic in one, and presumptively similar in the other. The first patient was found to have an invading carcinoma low in the colon, while in the second, the precise nature of the colonic lesion could not be determined. In both patients at necropsy, the abscesses in the liver were large, with a tendency to be multilocular. The exudate was predominantly purulent, although it might appear caseous in the smaller lesions, and it also had a peculiar putrid odor like that of butyric acid. In the gross differentiation from amebic abscesses, it is pointed out that the latter are usually solitary and unilocular. Actinomycotic abscesses frequently have extremely heavy capsules, while staphylococcic and streptococcic abscesses are often associated with suppurative pylephlebitis, and have an even more distinct multilocular appearance.

In their bacteriologic studies, the authors point out the difficulty with which these organisms are made to grow on artificial media, which must at least be enriched by the addition of blood, serum, or tissues. Marked variations in morphology occurred, depending on the age of the culture and the type of the medium; the most marked aberrations having occurred on solid media. The forms observed were chains, coccobacillary forms, filamentous forms, rods, and rods with large bulging granules. The species Funduliformis, is always gram negative and non-motile.

Following the description of subcutaneous abscesses produced by inoculation into guinea pigs and rabbits, the authors summarize the pertinent facts by stating that infections of this type are probably not uncommon, and that the two outstanding regions of primary vulnerability are the large bowel and the male genito-urinary tract. From such sites (which may be cryptic) dissemination is hematogenous to the liver and the lungs, with an interval bacteremia which is, or should be clinically demonstrable. The infections are very severe and the outcome should be viewed with gravity.

H. J. Wolff.

LEVY, J. S.

The Value of a Neutralization Test of Gastric Acidity in Patients with Duodenal Ulcers and So-called Pylorospasm. Annals of Int. Med., 7:1244, (April) 1934.

The author finds that a neutralization test with an acid meal gives results which may be used to distinguish normal from abnormal cases (duodenal ulcer and pylorospasm secondary to pathological appendix). In the latter cases the neutralization is both diminished and prolonged. The results after the neutralization are more uniform and furthermore the test is based on sound physiological principles.

Samuel Morrison.

SHAY, H. AND SCHLOSS, E. M.

A consideration of the Gastric Ulcer-Cancer Problem. With the Report of a Case of Ulcerating Carcinoma in which the Gastric Acidity Changed from Normal to Anacidity While Under Observation. Annals of Internal Medicine, 7:1218, (April) 1934.

These authors believe that the more reliable figures, obtained by tracing the after history of those cases of gastric ulcer that have been treated by gastro-enterostomies, would speak eloquently against any high incidence of cancer engrafted upon simple ulcer. In making an early diagnosis of cancer of the stomach the duration of symptoms is of value since the history is short as contrasted with the comparatively long history in ulcer but the authors do not believe that a long history is justifiable presumptive evidence of ulcer-cancer. They also feel that anacidity, while frequently present in cancer, does not exclude its possibility when absent. The authors do not subscribe to the view that cases of gastric carcinoma in which acid persists, develop on an ulcer basis and they stress the presence of duodenal ulcers in some cases along with the gastric lesion. In such instances the duodenal lesion may be responsible for the acid reading. They note that of the numerous theories suggested to explain the relatively high incidence of anacidity in gastric cancer, that of an associated gastritis appears most logical and receives the greatest support. Contrary to others, the authors, believe that an ulcerating gastric lesion, associated with an anacidity is presumptive evidence in favor of carcinoma as against non-malignancy. Persistent occult blood in the gastric contents even after the patient has been under treatment favors the diagnosis of malignant ulceration. The position of the lesion in the roentgen ray study is of more value than the size or form of defect. Of all the criteria mentioned the authors place the greatest stress upon the disappearance of occult blood reaction in the gastric contents since the other improvements may occur with a malignant as well as a benign ulcer. They report their case in which free hydrochloric acid disappeared during the progress of a carcinomatous ulcer.

Samuel Morrison.

PRICE, A. E. AND SCHOENFELD, B. J.

Felty's Syndrome—Report of a Case with Complete Postmortem Findings. Annals of Int. Med., 7:1230, (April) 1934.

The authors conclude that the symptom complex of arthritis, splenomegaly and leukopenia is probably not a new disease entity but may be explained on the basis of a chronic infectious process.

Samuel Morrison.

FINKELSTEIN R. AND JACOBI, M.

Report of Two Unusual Cases of Primary Carcinoma: (1) Primary Carcinoma in the Liver, with Cirrhosis of the Liver, Occurring in a Female. (2) Primary Carcinoma in the Jejunum. Annals of Int. Med., 7:1319, (April) 1934.

The authors point out again that the majority of cases of primary carcinoma of the liver are associated with cirrhosis of the liver. Both cases are rare enough to be reported.

Samuel Morrison.

BANKS, BENJAMIN M. AND BARGEN, J. ARNOLD

Relapses in Chronic Ulcerative Colitis Causes and Prevention. Archives Int. Med., 53, 131-139, Jan. 1934.

Recurrences in a series of 209 medical and 23 surgical cases of colitis have been studied for causative factors. Acute upper respiratory infection started attacks in 57%, over-exertion and emotional upsets in 13%. Conditions which traumatized, or increased the irritability of the gastro-intestinal tract such as improper diet, alcohol, abuse of laxatives, allergy, etc., in 12% and the removal of oral foci of infection, such as teeth or tonsils in 5%.

The incidence of recurrences was highest in the winter at the time of most respiratory infections, and lowest in the summer. Frequency of recurrences decreased with each decade of life. The situation and extent of the lesion did not influence the frequency of recurrences.

The prophylaxis of colitis in the quescent stage includes proper diet, avoidance of emotional and physical strain and the use of vaccines.

Franklin W. White.

RIVERS, ANDREW B.

Clinical Consideration of the Etiology of Peptic Ulcer. Arch. Int. Med., 53, 97-119, Jan. 1934.

An attempt is made to apply hypothesis of the cause of peptic ulcer to the clinical treatment of ulcer in man. Ulcer is probably the result of several interacting and variable factors. Physiologists have shown that undiluted gastric juice can produce ulcer by erosion. It does this more effectively when it acts on tissue unprotected by nature against it. This erosion is more likely to occur when the resistance of the exposed tissues is lowered by trauma of any kind such as infection or mechanical irritation. Systemic factors if they reduce the tissue resistance or increase the erosion of the acid chyme may make the development or recurrence of ulcer more likely. These causative factors vary in different persons at different times. A study of each case should show the factor or factors which are most important, and correction of these factors should give good results in the treatment of ulcer. This is illustrated by three groups of case histories showing respectively predominance of tissue trauma, acid erosion or systemic factors.

Franklin W. White.

BOYD, WILLIAM

The Relationship of Polycythemia to Duodenal Ulcer. From Am. Jour. Med. Sciences, May, 1934, p. 589.

A case of polycythemia with duodenal ulcer, thrombosis of the anterior descending branch of the left coronary artery, enlarged liver and spleen and ascites is described. At autopsy, two duodenal ulcers were found; one on the anterior wall and one on the posterior wall, the latter being the larger and apparently the more chronic. The liver weighed 2,200 gms., and the cut surface was that of chronic venous congestion.

Relationship between polycythemia and duodenal ulcer is discussed and the conclusion is reached that the polycythemia bore a causal relationship to the duodenal ulcer.

Allen A. Jones.

KEMP, HARDY A. AND HABERMAN, SOL.

Bacillary Dysentery in Dallas, Texas. Some Notes on the Etiological Agents. Am. Jour. Trop. Med., 14:191-193. March, 1934.

The authors have made stool cultures from 58 cases of bacillary dysentery occurring in Dallas, Texas, during the summer of 1933. Of these, 26 cases furnished cultures of dysentery bacilli, of which 16 were identified as *Shigella paradysenteriae* var. Flexner, 5 as *Shigella dispar* Andrewes, and 5 as *Shigella paradysenteriae* var Sonne. Relative inagglutinability of the Sonne types was demonstrated. No Shiga types of dysentery bacilli were demonstrated in this series.

Col. Chas. F. Craig.

REED, ALFRED C. AND JOHNSTONE, HERBERT G.

Amebiasis Among One Thousand Prisoners. Final Report. Am. Jour. Trop. Med., 14:181-189, March, 1934.

The authors detail the results of the examination of stained preparations from the stools of 1,000 prisoners at San Quentin Prison, California, for *Endamoeba histolytica*. Of the 1,000 prisoners, 92, or 9.2 per cent were positive for *Endamoeba histolytica*. Of these, 42 were treated with carbarsone, of which all but one remained negative for *Endamoeba histolytica* after completion of treatment, for periods varying from 3 to 7 months, being negative at the last examination, while of 31 treated with vioform all but one was negative for *Endamoeba histolytica*, the follow up periods varying from 4 to 7 months. The authors state "It is our belief that re-infection is more important than relapse and that the chief spread of amebiasis is by food-handlers."

Col. Chas. F. Craig.

ALVAREZ, W. C.

Abdominal Pain: II—The Sensitive Regions in the Abdomen and Ways in Which They May Be Stimulated to Produce Pain. J.A.M.A. 102:1351, April 28, 1934.

In this paper an effort is made to understand the mechanism of abdominal pain. "The main sensory pathways out of the upper part of the abdomen lie along the major splanchnic nerves. Most of the sensory nerves in the abdomen probably do not belong to the autonomic system and are no different from those in the rest of the body. Evidence is accumulating to show that certain types of severe and intractable pain are due to some abnormality in the sympathetic nerves.

The abdominal viscera are insensitive to such stimuli as cutting, crushing and burning. The few sensory nerve endings present are associated mainly with arteries. The parietal peritoneum is everywhere well supplied with nerves. If a stimulus to an abdominal organ is to be sensed as pain, it must be applied over an area wide enough to affect many of the scattered nerve endings."

The author discusses separately the various abdominal organs and their possible mechanisms of pain production. He throws out the suggestion that some forms of abdominal pain may be due to the accumulation of irritant metabolites or toxins in the tissues.

Samuel Morrison.

MORAWITZ-MANKE.

Secondary Pellagra. Archives f. Verdauungskrankheiten, January, 1934, Vol. 55, No. 1-2.

Europe is not free either from this disease. The case reported showed an achylia refractory to histamin associated with periodic diarrhoeas. Stool examination was negative to flagellates and protozoa but it revealed a poor absorption of fats. Blood chemistry was normal, the nitrogen content of the stool could not be determined. Diagnosis was attained by the dermatological findings which consisted of symmetrical and bilateral hyperkeratoses of both hands and face associated with seborrhea and papillitis of the tongue interspersed with atrophic and flaming red areas ("Himbeerzunge"). There was a psychosis (maniac depression) present without any pathological neurological findings. It is assumed that severe alterations in the gastro-intestinal tract are responsible for this condition with possibly a poor absorption of Vitamin B2 contents.

M. E. Gabor.

WEBSTER, D. R., AND J. C. ARMOUR.

Effect of vitamin deficiency on gastric secretion. Proc. Soc. Exper. Biol. and Med. 30:1297-1300 (June) 1933.

The experiments reported here indicate that the vitamins contained in yeast are necessary for the normal secretory activity of the gastric mucosa. No analyses have yet been made of the B fraction responsible for this effect. The complete achlorhydria under the condition of avitaminosis was obtained independently of anorexia and inanition, which never occurred in the experimental animals.

L. T. C.

SECTION II—*Experimental Physiology*

THE INFLUENCE OF THE PYLORUS UPON THE REGULATION OF THE ACIDITY OF THE GASTRIC SECRETION*

By

WILLIAM WALSH LERMANN, M.D.

and

LYLE M. NELSON, JR., M.D.

PITTSBURGH, PENNSYLVANIA

THE following detailed work, is an attempt to ascertain the significance of the pyloric mechanism in the control and regulation of gastric acidity. For many years it has been apparent that the secretory findings were dependent not alone on native acidity or the dilution factor but that, in some way the alkaline, pancreatic secretion played a *role*. It is apparent in a survey of the literature that many authors have referred to the significance of the pylorus in this mechanism.

Cannon's early theory of the mechanism of the pyloric function was based on his contention that the appearance of acid at the pylorus causes the sphincter to relax and that the appearance of acid in the duodenum results in closure of the sphincter until the acid is neutralized by the alkaline pancreatic juice, after which the process is repeated until the stomach is empty. This theory has been proven incorrect by the work of Baird, Campbell and Hern who point out that gastric and duodenal intubation show that acid in the duodenum does not necessarily close the pylorus, for the most rapid emptying time took place where the duodenal contents were unusually acid. Furthermore, an acid stomach shows a similar tendency to premature evacuation. Ivy found that strong acids or alkalies in the duodenum most frequently cause relaxation of the sphincter and regurgitation of duodenal contents (bile) into the stomach.

Stimulation of the plexus of Auerbach causes contraction of the intestinal wall above and relaxation below; this is the "Law of the intestine" (the myenteric reflex). In 1899, Bayliss and Starling reported that handling the intestine with the fingers "produced reflex inhibition of the whole length of the intestine."

Cannon, later, concluded that the inhibition reflex of the stomach travelled mainly *via* the extrinsic nerve but could travel equally well *via* the intrinsic nerve. Later he observed that section of the intestines eighteen inches below the pylorus caused the pylorus to remain in spasm five hours.

Pearcy and Van Liere determined that distention of any portion of the gastro-intestinal tract will produce inhibition of every other portion of the tract; the part stimulated will respond by contraction.

Carlson and Litt proved that the motor disturbances of the pylorus may be induced not only by local pathological conditions in the stomach and the duodenum, or by abnormal states of the central nervous system, but also by excessive irritation of most, if not all, sensory nerves, particularly those of the abdominal organs. Ryle decided that the important factors promoting pathologic hyperacidity were an excessive secretion and pyloric hypertonicity. Apperly believes that the positive forces of the duodenum normally play a part in the regulation of the alkali reflex. Bolton, Goodhart and Campbell all conclude that the pylorus is the main factor controlling the duodenal reflex. Brunemeier and Carlson show that stimuli in the duodenum call forth contractions of the pylorus and induce, at the same time, inhibition of the tonus and contractions of the empty stomach. Cole, by serial X-ray studies, has demonstrated that the activity of the pyloric sphincter is directly proportional to the magnitude of the antral contractions and that chyme passes into the duodenum during gastric systole but not during diastole. The work of Alvarez, Thomas and Wheelon, Luckhardt, Phillips and Carlson support the neuro-muscular control of the sphincter.

Boldyreff propounded the theory of the "automatic" regulation acidity of the contents of the stomach. This theory maintains that the initial high acidity of the gastric juice is lowered to the acidity of 0.15 to 0.021 HCl by an influx of intestinal juice into the stomach with the purpose of neutralizing the superfluous acidity; a portion of the strong acid fluid passing from the stomach into the intestines produces a combined secretion largely of pancreatic juice—and if there is not sufficient pancreatic secretion, there are also bile and intestinal juices secreted which provide the necessary material—the acid fluid, according to this author, irritates the intestinal wall, provokes antiperistalsis which then drives the alkaline secretion of the duodenum into the stomach, resulting in the lowering of the acidity of the contents to the usual level of 0.16 HCl. This theory has been confirmed by Migas, Milosoron, Carlson, Ehrenreich, Spencer and others. It is further believed that hyperacidity probably is due to the fact that there is a disappearance of this protective, regurgitation mechanism. Thomas and Wheelon produced experimental evidence to show that the pyloric sphincter receives a double nerve supply consisting of motor and inhibitory nerves, coursing by way of the vagi and splanchnics, both nerves being mainly motor in function.

The recent work of Stevens adds important evidence to the neutralizing powers of the duodenal contents. Working on dogs, he reports quantitative studies on uncontaminated duodenal juice *in vivo*, which investigations show conclusively that the duodenum, before isolation, can neutralize an average of 1800 c.c. of 0.5 percent hydrochloric acid during a day in addition to the acid passing through the pylorus; these figures suggest that it has a reserve function in this respect considerably in excess of physiologic needs.

It would appear that Stevens' work shows the neutralizing powers of the duodenal contents to be even greater than we imagined; recalling the "Law of the intestine" and the reports of Carlson and Litt that "Motor disturbances of the pylorus

*Department of Gastro-Enterology, The Western Pennsylvania Hospital, Pittsburgh.
Submitted for publication, April 18, 1934.

may thus be induced not only by local, pathologic conditions in the stomach and the duodenum, or by abnormal states of the central nervous system, but also by excessive irritation of most, if not all, sensory nerves, particularly those of the abdominal viscera." still we are without proof of the neutralizing effect of reflux duodenal contents *in man*, as the experimental physiological surgery on dogs immediately calls into action the pyloric contraction (the law of the intestine).

METHOD AND SCOPE OF AUTHORS' STUDIES

Variations in successive fractional gastric analyses may be noted on the same patient. These variations were at times too great to be explained by medication and diet, so that a study of the component parts, other than the acids, was made. The presence of and the quantity of bile and trypsin were noted in the lower acid analyses to be much more frequent and greater in amount than in those with higher acid response.

In order to obtain added information as to the control and the effect of the regulation of acid secretion in the digesting stomach by the regurgitation of the duodenal contents, the following test was made: A Rehfuss gastric tube was changed to a gastro-duodenal tube by changing the metal bulb or tip into two distinct parts; this was done by sawing the tip laterally at its midpart and inserting a solid bar, thus dividing it into two parts not connected by any passage way or opening; both ends of this tip were perforated and rubber tubing connected, the lower end having a tube six to eight inches in length, to be changed according to the position of the stomach in each patient. A regulation Rehfuss bulb was attached to the shorter piece of tubing. (Figure 1).

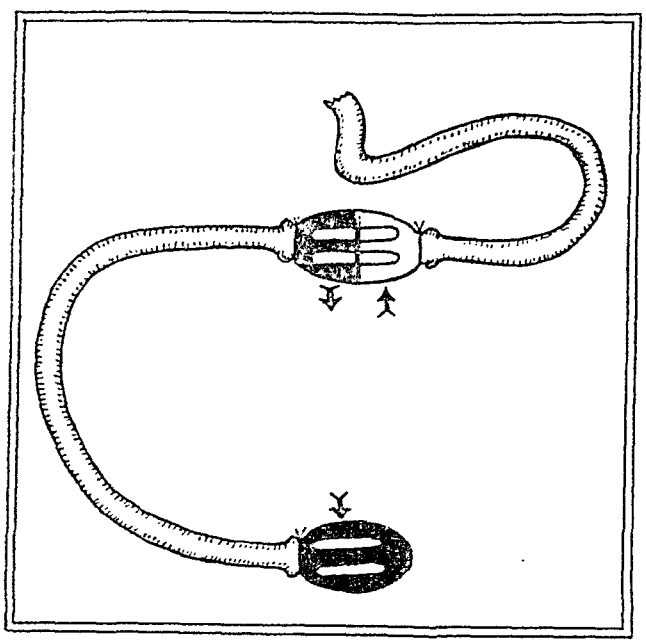


Figure 1—Lermann modification of Rehfuss tube for Gastro-Duodenal studies.

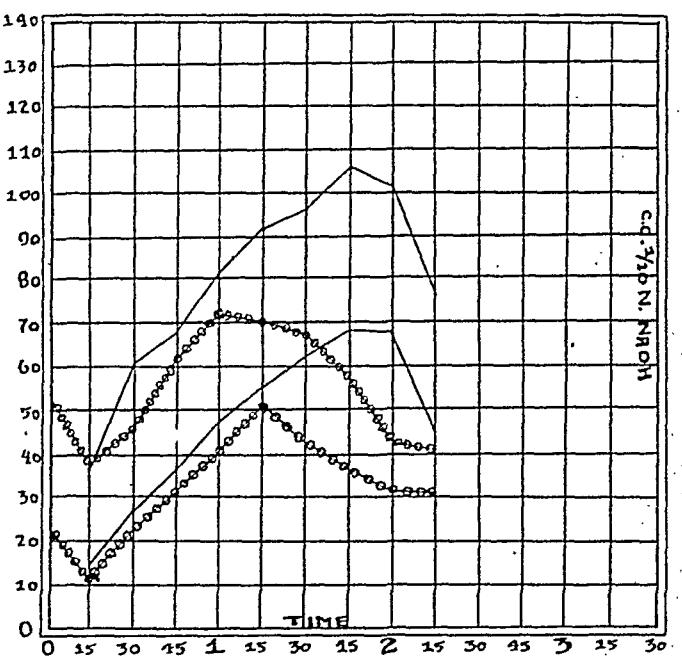
Twelve cases of clinical duodenal ulcers were studied, all of whom showed a high fractional acid content 24 hours prior to the gastro-duodenal test. This gastro-duodenal tube was swallowed in the early morning after approximately 15 hours' fast; it was then observed under the fluoroscope at 15 minute intervals until the duodenal bulb was seen to be in correct position in the duodenum. When this was accomplished, a test meal of tea and toast was given and contents withdrawn for analysis at 15 minute intervals. All duodenal contents regurgitated had to pass through the perforations in the lower half of the gastric bulb and mix with gastric contents before being aspirated for analysis.

The regurgitation of bile and trypsin was very noticeable in all specimens during the gastro-duodenal test, although these had been absent in most of the fractional gastric analyses previously made on these patients. The lowered acid content was marked in all but two of these cases and these had shown large amounts of bile and trypsin in the fractional analyses done previously. By this method, any influence of the pylorus in preventing the reflux of the alkaline duodenal secretion was obviated and the pylorus held open by this tube permitting the free regurgitation of duodenal contents during gastric activity. Our findings lend support to the work of Alvarez, Bolton, Carlson, Cannon, Cole, Crohn, Rehfuss, Ryle and others concerning the dominant part played in gastric function by the pylorus and the duodenum.

One of the most interesting points regarding our work-curves is that they represent a series of observations on clinical duodenal ulcer. In practically every instance the fractional gastric curve is typical of that condition, showing the high step-ladder rise and follow-through with high free acid. With few exceptions, this is the type of curve which is depicted on these charts in a single fractional tube examination.

When the gastro-duodenal tube is inserted, however, in the majority of instances, the contour of this curve definitely is altered. This can be far better appreciated if the general average of twelve cases is carefully analyzed.

In Chart 1, which shows perhaps better than any other, the general findings and which is representative of a composite group, one notices first the typical form of composite curve for duodenal ulcer. Then on studying the broken line, he observes that the broken line follows an almost normal



°°°°G. D. Tube in position. —Single tube—fractional

Chart 1—Average of 12 Cases of Duodenal Ulcer

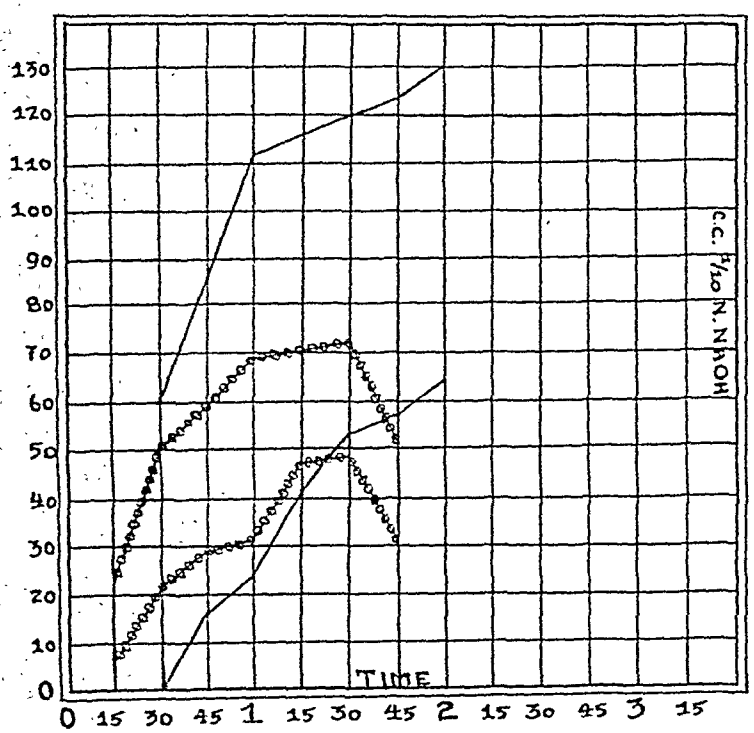
curve for one hour. To one's surprise, the duodenal ulcer curve is normal for the first hour, a fact which to our knowledge has never been brought out in the literature. Generally it is believed that the duodenal ulcer curve is an abnormal curve in every respect. Our studies show, however, that when the pylorus is kept open, the curve turns sharply downward and follows more or less the normal curve. It is striking that the abnormal portion of the duodenal ulcer curve is in the second hour and it is precisely this portion which is modified by the technic that has been used. One cannot escape the conclusion that, in some way, increasing tonicity of the antral and pyloric segment is probably responsible for this change.

Some of the graphs of the acid curve are of great interest, showing conclusively the secretory change produced by this method of controlling two factors which have long been

known to be of prime importance in the regulation of gastric secretion. First, one must realize that this tube blocks pyloric closure and thereby minimizes the muscle tonicity of the antrum and pyloric segment; second, we are convinced that the free regurgitation of duodenal contents is a factor which is naturally controlled by the tonicity of the antral and pyloric segments, but which plays some part in what may be termed the "chemical control" of gastric secretion.

While the average reduction in acidity in our 12 cases shows the free reflux of duodenal contents to lower the total acid in 1½ hours 38 points and free hydrochloric acid 20 points, some cases such as case 7 (here illustrated, Chart 2), shows at the 1½ hour period 50 points total acid and 5 points free hydrochloric acid; the maximum reduction at the 1¾ hour period is 83 total, 38 free hydrochloric acid.

The consensus of opinion today is in support of the importance of the motility and emptying time of the stomach rather than upon the secretory function in the causation of

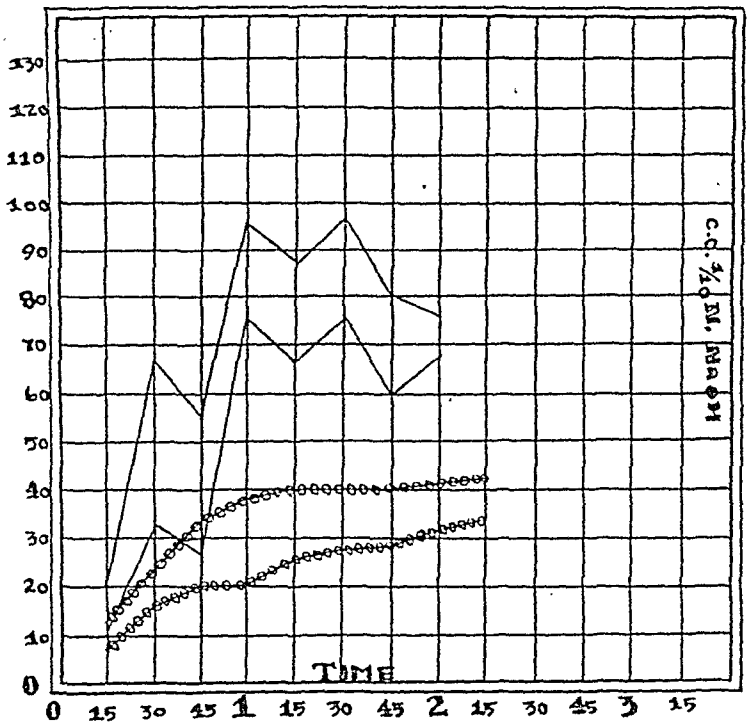


°°°°G. D. tube. Tips shown in correct position by fluoroscopic control. Bile, positive in all specimens. — Fractional—single tube. Bile, trace in all specimens

Chart 2—A.S. Case No. 7

gastric pathology and resulting symptoms. Bolton states that symptoms constituting dyspepsia are not primarily due to alteration in the secretion of gastric juice, or in the chemical process of digestion, but to alterations in the motor function of the stomach. So long as these functions are conducted normally, and the stomach empties in normal time, it does not matter whether the gastric juice is increased or diminished in amount, but if the stomach fails to empty itself normally. then secondary alterations occur in the gastric contents, which add to or modify the symptoms produced by the motor insufficiency of the stomach. Carlson has shown that "hunger pains" are due to excessive contractions of the pylorus and pyloric end of the stomach.

To summarize the work published on the function of the pylorus and on duodenal regurgitation, Rehfuss concludes that one group of observers would make the function of the pylorus dependent entirely on the neuromuscular mech-



°°°°G. D. tube. X-ray taken and on file. Bile—positive in all specimens. —Fractional—single tip tube. Trace of bile in all specimens.

Chart 3—H.B.H. Case No. 4

anism; another group of workers would emphasize the great value of acidity of the gastric juice; another series of studies would emphasize the importance of the distention and filling of the duodenum and, still others, would emphasize the importance of the distention and filling of the lower bowel. He himself concludes that the movements of the pylorus are controlled by reflexes arising in the mucous membrane of the stomach and the duodenum, and agrees with Ryle, who points out that where a relationship between the secretory phenomena and the emptying time is discernible, it is just as reasonable to regard the high or low acid as the *result* and *not the cause* of pyloric hyper- or hypotonus.

This experimental work appears to add more conclusive proof to the previous original studies and the literature published. Future studies following this preliminary report will deal with the relationship of duodenal contents, trypsin, bile, etc., and the gastric secretion.

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ABSTRACTS

BLALOCK, ALFRED, NASHVILLE, TENNESSEE.

Acute Circulatory Failure as Exemplified by Shock and Hemorrhage. S. G. & O., Volume LVIII, March, 1934, Number 3, pages 551-566.

The author classifies acute circulatory failure from a physiological viewpoint into five groups, i.e., 1. Haematogenic type; 2. Neurogenic type; 3. Vasogenic type; 4. Cardiogenic type; 5. Unclassified conditions; this grouping is based chiefly on the physiology resulting from different etiological factors.

According to Groeningen, James Latta in 1795 was the first to employ the term "shock" with the meaning that is now attached to it. The author cites two excellent descriptions of clinical shock by describing two acutely shocked patients both going to post mortem and showing no visible change in any vital organ.

A thorough historical resume reviews briefly the fundamental work on shock by such men as Ambroise Pare, W. Clowes, 1568, Wiseman in 1719, Garengiot 1723, John Hunter, Bichat, Travers, Samuel Gross, Goltz, Billroth, Groeningen, Henderson, Cannon, Crile and Phemister. An important advance in the development of the present conception of shock was made in 1879, when Mapother stated that the most marked physical change caused by shock was a contraction of the arterioles. He assumed that the dilator nerves were paralyzed.

The author mentions that primary shock occurs immediately following receipt of the injury, while in secondary shock there is an interval of one hour or longer between the injury and the development of unfavorable symptoms.

Numerous experiments were performed on dogs—where injury was produced by striking one of the posterior extremities of deeply anesthetized dogs numerous blows with a hammer. These experiments showed that severe trauma with rupture of large vessels results in loss of blood of some composition as it exists in the blood stream and a dilution of remaining blood occurs. Milder trauma causes loss of greater proportion of plasma than of red cells and a resulting concentration of blood occurs.

Parsons and Phemister concluded that reflex vasomotor paralysis or exhaustion did not account for the circulatory failure, since intensive stimulation of somatic nerves produced elevation instead of fall in blood pressure.

The author's experiments on dogs showed that if he lowered the blood pressure by removal of blood and that if the blood pressure remained at a low point for several hours, transfusion was without benefit. If the blood pressure remains depressed for a considerable time, the vaso-constrictor mechanism fails and vasodilatation results. An increase in concentration of red blood cells was found in all these experiments.

The author feels that there are contributory factors that play a part in the production and maintenance of shock.

In the prevention of shock it should be remembered that a person may have lost a great deal of blood and still have an essentially normal blood pressure, but yet the loss of a slight additional quantity may result in severe shock. It is important to realize that the aim in treating secondary shock is not to produce a high blood pressure but to cause an increase in the volume of circulating blood. Special attention was devoted to the protein content of the blood plasma because it is the substance that attracts fluid into the blood stream and holds it—it was found that when whole blood was introduced intravenously in place of glucose or salt solution, there was not the decrease in the protein content of the plasma as was the case with the great loss of both fluid and protein plasma when only salt or glucose was injected. Addition of adrenalin and pituitrin had no effect on this loss of plasma.

Charles T. Sturgeon.

MILLER, T. GRIER AND ABBOTT, W. OSLER

Intestinal Intubation: A Practical Technique. Am. Jour. Med. Sciences, May, 1934, p. 595.

The authors describe a double-lumened rubber tube with a Rehfuss bucket and a rubber bag attached at the distal end.

In the technique, the tube with the bag deflated is taken by the fasting subject in the morning, the subject reclining on the right side until the tube has reached the duodenum, the contents of which may be determined by its character obtainable through lumen B., or by fluoroscopic observation. A special posture is no longer required. When the capsule has reached the third portion of the duodenum, the bag is distended moderately with air or an 8% sodium iodide solution for visualization. Then 5 cm. of the tube is swallowed every ten minutes until the desired point is reached. In six hours the tube usually passes to a distance from 120 to 150 cm. beyond the pylorus. Einhorn estimated the length of tubing required to reach from the pylorus to the cecum was approximately 270 cm.

The authors have investigations regarding chemistry and physiology of the small bowel under way, also studies upon the motor effects of drugs administered orally or by lumen B, or hypodermic injection, also Roentgenray study of duodenal lesions and bacteriologic study of the contents of the small bowel under fasting conditions and after the administration of certain types of food.

Allen A. Jones.

HAWKINS, WILLIAM B. AND WRIGHT, ANGUS.

Bile Plasma Cholesterol: Fluctuations Due to Liver Injury and Bile Duct Obstruction. J. Exper. Med., 59:427-439, April, 1934.

The authors, working on dogs, substantiate the claims of Feigl, Epstein and others that chronic liver injury caused by chloroform brings about a hypocholesterinemia with drop in the cholesterol esters from a normal ratio (40% to 70%) to 30% or less. They also confirm the findings of many others that prolonged biliary obstruction produces a hypercholesterinemia, and suggest that these facts may have a clinical application in differentiating obstructive liver disease and parenchymal liver disease.

Martin Vorhaus.

WRIGHT, ANGUS AND WHIPPLE, GEORGE H.

Bile Cholesterol: Fluctuations Due to Diet Factors, Bile Salts, Liver Injury and Hemolysis." J. Exper. Med. 59:411-425, April, 1934.

Experiments in bile fistula dogs show, under uniform diet conditions in a normal animal, a constant excretion of cholesterol, i.e., 0.5 to 1 mgm. per kilo per 24 hours. Diet rich in egg yolk will increase cholesterol in the bile (5 to 15 mgms.) but considerably less than the amount of cholesterol intake. Bile salts alone will increase cholesterol output in the bile as much or more than a cholesterol rich diet. Mild moderate liver injury (chloroform) markedly diminishes the bile salt and cholesterol content of the bile. Decholin and isatin increases bile flow but causes no change in cholesterol elimination.

Martin Vorhaus.

GROSS, ERWIN G. AND SLAUGHTER, DONALD H.

The Action of Paparerine on the Muscular Activity of the Alimentary Canal. Journal of Pharmacology and Experimental Therapeutics, 43 (3): 551-562, November, 1931.

In view of the constant search by gastro-enterologists for drugs which will relax the bowel, it is interesting that Gross and Slaughter found, in the stomach, that papaverine reduced the tone level and abolished peristaltic waves. In the small intestine, subcutaneous, intramuscular, and intravenous injections of from 1 to 10 mgm. per kilogram body weight of papaverine failed to influence the motility in any consistent manner. In the colon, papaverine decreased the frequency of the tone waves without changing the general tone level but this effect was slight.

Walter Alvarez.

CRISLER, GEORGE, VAN LIERE, E. J., AND BOOHER, W. T.

The Effect of Anoxemia on the Digestive Movements of the Stomach. Am. J. of Physiol., 102 (3): 629-634, December, 1932.

VAN LIERE, E. J., CRISLER, GEORGE, AND ROBINSON, DENNIS.

Effect of Anoxemia on the Emptying Time of the Stomach. Arch. of Int. Med., 51:796-799, May, 1933.

In view of the well-known fact that a failing heart will often cause indigestion, two papers by Van Liere and his associates are of interest. They produced anoxemia in dogs and found marked inhibition of gastric movements, together with a considerable degree in delay of emptying of the stomach. Obviously, there can be several other ways in which a failing heart can influence the digestive tract. It can influence it through the nervous system, and it is conceivable that it can produce flatulence through changing the tension of gases in the blood.

Walter Alvarez.

ALLES, GORDON A.

The Physiological Significance of Choline Derivatives. Physiological Reviews, 14:276-307, April, 1934.

Alles discusses the historical development of our knowledge of choline and its derivatives, particularly acetylcholine, muscarine, carbaminosylcholine, and acetyl B methylcholine, with particular reference to their participating as humoral agents in intestinal, cardiac, ocular, vasodilator and voluntary muscles, and vasodilator, secretory, and sympathetic mechanisms. In regard to the intestinal mechanism it is pointed out that from the isolated intestine of the rabbit there diffuses out into its enviromental saline as much as 3-4 mgm. of choline in an hour. In addition, the intestine has the power of synthesizing choline and acids to form esters, and it also contains an enzyme which is capable of destroying acetylcholine and therefore capable of accelerating its synthsis. The intestine contains relatively large amounts of this enzyme. Stimulation of the vagus increases the quantity of free active agent in the intestine. The action of muscarine and acetylcholine is apparently upon some receptor mechanism or substance distinct from the nerve ending. A more recently popular derivative acetyl B methylcholine has been suggested for trial as a useful drug for specifically stimulating the parasympathetic nervous system because of the duration of its effects and its freedom from appreciable nicotine-like activities. Subcutaneous doses of 5 mgm. produce definite cardiovascular alterations. 50 to 100 times this dose has to be administered orally to produce effect, and this was slow in onset and mild in degree, suggesting a marked degree of destruction during absorption. Gastro-intestinal effects were more evident than cardiovascular changes with oral administration in contrast to subcutaneous administration.

Dwight Wilbur.

SMITH, ELIZABETH R. B.

Gelatinase and the Gates-Gilman-Cowgill Method of Pepsin Estimation. Jour. of Gen. Physiol., 17: 35-40, September 20, 1933.

The author using pure canine gastric juice from a Pawlow pouch determined that the enzymatic activity of this fluid is the same whether measured by the gelatine film method or by the hemoglobin technique of Anson and Mirsky. Higher values are obtained by the gelatin viscosity method, suggesting the presence of some gelatinase activity in this material. It is believed that the gelatine film method constitutes as nearly a truly peptic method as does any other.

Dwight Wilbur.

GAVIN, G., MCHENRY, E. W. AND WILSON, M. J.

Histamine in Canine Gastric Tissues. (J. Physiol., 79,234-238). 1933.

Since the work of Popielski, showing that histamine will cause a gastric secretion, the question has been raised whether histamine is the gastrin isolated by Edkins from the pyloric mucosa of the stomach. Ivy and his co-workers found that histamine isolated from the hog's stomach is inactivated by histaminase. The present workers go further into the problem and make a study of the distribution of histamine in the gastric tissues.

It is significant that, whereas Edkins found that fundic extracts do not produce a secretion, these authors find that they do.

The extracts were assayed on the blood pressure of a cat against the effects of a standard histamine solution. All the extracts lost their secretagogue and depressor effects when incubated with histaminase; they did not contain choline, "callicrein," etc., so that the active principle is probably histamine.

There is always more histamine in gastric mucosa than in gastric muscle, and about two hours after a meal the histamine content is greater than in a starving animal. Eighty per cent of the total histamine of the stomach is present in the fundic mucosa, whilst only 12% is in the pyloric mucosa.

M. H. Friedman.

SCHAROWATOWA, O. F.

Pflugers Archiv 234, No. 1, 124-129, (Feb. 1934). Zur Frage des Mechanismus der zweiten Phase der sekretorische Magenfunktion. (The mechanism of the second phase of gastric secretion).

Complete resection of the pylorus was performed in 3 dogs equipped with Pawlow pouch, the continuity of the gut being restored by gastroduodenostomy. The pouch secretion in response to standard meals (bread, milk, meat, Liebig's extract) was studied before and after the operation. Volume, duration of secretion, and acidity remained practically unchanged; there was a slight increase in peptic power. The author concludes that contact of food with the pyloric wall is not an essential condition for the second phase of gastric secretion: this phase is therefore due to absorption of secretagogue bodies derived from the food, rather than to a specific hormone "gastrin" released from the wall of the pylorus.

F. C. MacIntosh.

KOSKOWSKI, W.

Journ. de Physiol. et de Path. Gen. 31, No. 3, 697-712, (Sept. 1933). Les propriétés dynamiques du sang au cours de la digestion et leur changements dans différentes conditions experimentales. (The dynamic properties of the blood during digestion and their changes in various experimental conditions.)

Blood withdrawn from dogs or human subjects during digestion of a protein meal contains a histamine-like substance, as shown by its action on the isolated virgin guinea-pig's uterus. Blood withdrawn from fasting subjects or during digestion of fat or carbohydrate does not possess this property. The author considers that the second phase of gastric secretion is evoked by histamine, but gives no direct proof of its identity with the uterus-contracting substance of blood.

F. C. MacIntosh.

BARCLAY, A. E.

The Mechanics of the Digestive Tract. Lancet 226, Jan. 6, 1934.

The normal mechanism of the propulsion through the alimentary tract can only be seen under normal conditions by radioscopic methods. Normal movements depend on the free mobility of the viscera. Under restricted conditions or when the abdomen is opened such movements as are seen are likely to be reserve mechanisms or distortions of normal movements. Radioscopic observations suggest that in the majority of cases, the movement of the bolus from fauces to the upper part of the oesophagus, is due to the negative tension in this part and that the food is sucked down rather than the propulsion method described in the textbooks. This latter method is a reserve mechanism used only to swallow dry or unpleasant food. Radioscopic observations suggest that in the upper part of the digestive tract peristalsis is a reserve mechanism: under normal circumstances the food is propelled by other means, such as increased tonic action and movements of the mucous membrane, perhaps aided in some parts of the tract by the development of negative pressure ahead of the oncoming food. In the lower part of the tract there is no rhythmic peristalsis but only occasional and infrequent projections of the contents through considerable lengths of intestine.

J. J. Day.

KUNITZ, M. AND NORTHROP, J. H.

Inactivation of Crystalline Trypsin. The Journal of General Physiology, 17: 591-615, March 20, 1934.

Trypsin, like other enzymes, becomes inactive in solution, and the rate at which this inactivation occurs depends upon the temperature, the pH, the concentration, and the purity of the solution. While crude trypsin preparations have a maximum stability at about pH 5.0 and are completely and permanently inactivated if heated above 70 degrees C., solutions of pure crystalline trypsin may be heated to boiling (in acid solution) for a short time without permanent loss in activity. The crystalline preparation is apparently a pure protein. The inactivation of crystalline pepsin may be reversible and irreversible. There is loss of activity at high temperatures or in alkaline solutions. In general, the decrease in activity under all these conditions is proportional to the decrease in the concentration of the trypsin protein.

Dwight Wilbur.

ANSON, M. L. AND MIRSKY, A. E.

The Estimation of Trypsin with Hemoglobin. Jour. Gen. Physiol., 17:151-157, November 20, 1933.

The formation from hemoglobin of split products not precipitable by trichloracetic acid is taken as a measure of tryptic activity. The split products are estimated colorimetrically. The authors note that many estimations may be made in a short time. The results are entirely reproducible. The hemoglobin solution keeps for some time and the rate of digestion is not sensitive to considerable amounts of acid, alkali, urea, or glycerol added to the enzyme. The method has several disadvantages also.

Dwight Wilbur.

NOTICE

Inasmuch as there have been numerous complaints of non-receipt of the Journal being received by the publishers, we would appreciate subscribers reporting at once this or other dissatisfactory experiences.

SECTION III—*Nutrition*

A STUDY OF OBESITY IN AN OUTPATIENT CLINIC*

By

EDGAR C. BECK, M.D.

and

ROGER S. HUBBARD, Ph.D.

BUFFALO, NEW YORK

THE treatment of obesity at the present time is showing two tendencies, one based on scientific reasoning and one on popular fancy. The work of Joslin and the experience of insurance companies show the importance of the subject and the need for intelligent study directed toward the control of the condition. The interest of the lay public in self-treatment, stimulated largely by women's desire to become thin in an effort to be stylish, has led to the development of various freak diets which have often proved harmful. It is evident that there is every reason for the study of proper methods of treating obesity and also for means of instructing the public in their use.

For a convenient definition of obesity we have chosen the one given by McLester.[1] "Obesity is a condition of the body in which the weight, because of the excessive storage of fat, is above normal." According to McLester's conception, the height-weight-age tables give only an approximation of normal weight and allowances can be made of 10% or more either above or below the accepted normals for adaptation to type of build, occupation, and other factors.

There are two reasons why the markedly obese person presents a distinct medical problem. He has certain symptoms and physical signs which greatly reduce his economic efficiency and his sense of well-being, and his life expectancy is less than is that of the average person.

In an analysis of the causes of death of 26,000 insured persons made by the Connecticut Mutual Life Insurance Co.,[2] it was found that heart disease accounted for the deaths of 15% of the "stout" as compared with 6% of the "lean." Other circulatory diseases caused 7½% of the deaths in overweights against 3% in the thin. Nearly twice the number of heavy, as opposed to light, people die of kidney disease.

Rollo Britten,[3] in the United States health reports for August 1933, gives the following figures in an analysis of 100,000 overweight individuals. The death rate was higher in fat people than in the thin in pneumonia; influenza, heart disease, cirrhosis of the liver, Bright's disease and apoplexy. There was an immense increase in high blood pressure in the obese group. The only diseases which were more prevalent in the lean were tuberculosis, diseases of the nervous system and diseases of the gastro-intestinal tract, not attributable to gall bladder disease.

Joslin[4] states that "diabetes largely is a penalty of obesity; the greater the obesity, the more likely nature is to enforce it." (i.e. the penalty).

Dr. Alonzo Taylor[5] explains why obesity is common in the United States. He says that the average amount of physical work done by the American man and woman is declining each year because of the mechanization of society, both in industry and in the home. This, plus the improvements in transportation, communication and business methods, has greatly reduced the bodily labors of living. Improved heating systems have lessened the energy necessary to keep warm. These would be good features, but unfortunately the average person's appetite has not been reduced in proportion.

Every clinic today has to contend with the problem of those who are receiving emergency economic relief and who therefore cannot afford to buy a wide variety of food. One would expect that such people would lose weight. On the contrary, the less expensive diets contain a great number of calories. Bread and spaghetti are the two cheapest sources of sustenance and many who have been forced to economize on their foodstuffs in the past three years have gained a considerable amount of weight.

The exogenous theory, which maintains that all cases of obesity are due to overeating and underexercising, is advocated by such investigators as Newburgh, [6] Johnston, Benedict,[7] Wilder, Smith and Sandford,[8] and Peters and Van Slyke.[9]

Newburgh[6] states unqualifiedly that obesity always is due to overeating. He says that even though some people maintain their weights or even gain while subsisting on a low caloric diet for as long as 16 days or more, eventually they will start to lose. Newburgh explains this phenomenon in the following way: "When undernutrition is effected by a diet low enough in carbohydrate to cause a large destruction of glycogen, the subject loses weight rapidly for several days while the body is giving up its glycogen, then abruptly enters a second phase during which there is a progressive retention of water by the tissues. After a number of days, this extra water is all given off and at the end of this third phase, the total loss of weight from the inception of underfeeding corresponds with the calculated weight of the tissue destroyed." He concludes that the failure to lose weight for the first week or more while actual tissue is being destroyed is due to the retention of water by the body.

Peters and Van Slyke[9] say that in all types of obesity, whether of known or unknown origin, one is forced to conclude that the immediate cause of the abnormal accumulation of fatty tissue is the ingestion of food in excess of metabolic needs. Any other conclusion, they state, would contradict the law of the conservation of energy.

The endogenous theory, which emphasizes the constitutional nature of obesity, is expounded by Silver and Bauer,[10] Bernhardt[11] and many other investigators.

Bauer[10] demonstrated the family incidence of obesity in 88% of his cases. He considers the exaggerated tendency of some tissues to store fat, water and salts, as the primary factor in the causation of the obese state and that this tendency is congenital and hereditary. He states that "obesity is not a result of overeating, but that overeating may be an inescapable consequence of an inborn tendency."

Many who favor the endogenous theory maintain that obesity is caused by a diminished specific dynamic action

*From the Outpatient Department of the Buffalo General Hospital, Buffalo, N. Y. Submitted for publication, April 21, 1934.

of protein. Ordinarily, normal persons respond to a protein meal with a 12 to 19% increase in metabolic rate. Plaut,[12] Grafe,[13] Wang, Strouse and Saunders,[14] and Bernhardt[15] state that the specific dynamic action of food is abnormally low in obesity, and that this is a primary characteristic and an important etiological factor. Benedict,[16] Wilder, Smith and Sandford,[8] Strang, McCluggage and Brownlee,[17] on the other hand, found no abnormally low specific dynamic action of food in the obese.

The cerebral theory assumes that a central nervous regulatory mechanism exists in the hypothalmus very close to the pituitary body. Supposedly, it controls the weight of man. Bernhardt[11] and Rony[18] are among the ardent advocates of this theory.

Recently, it has been expounded that in a small group of people, *obesity is caused by hyperinsulinism*. An excessive production of insulin by the pancreas leads to increased appetite and, therefore, to increased food intake, mainly in the form of carbohydrate. This causes the formation of increased fat deposits. Hyperinsulinism is always accompanied by low blood sugar. Two cases of spontaneous hypoglycaemia which came under the observation of one of us were extremely thin and had great difficulty putting on weight despite their increased appetites.

It can be perceived easily from the foregoing recapitulation that in obesity the question of *etiology* still is in a controversial state and that therefore it is difficult to obtain a suitable classification for the anomaly. Many classifications have been advanced, but none is entirely acceptable. Obesity has been classified on an etiological basis, on a pathological basis, on a symptomatic basis and some have attempted to classify it on a physical basis.

In 1929 and thereafter, a series of publications appeared by Evans, Strang and McCluggage,[19] advocating the use of extremely low caloric diets in the treatment of obesity. They reported that outside of upsetting the nitrogen balance of their patients for the first few weeks during which they were on the diet, no other obvious harm resulted and that their cases improved very markedly as these patients experienced their rapid loss of weight. The investigators hospitalized their patients during the course of treatment. However, the hospitalization for treatment of the average obese person generally is impractical because of considerations of time and money.

AUTHORS' OBSERVATIONS

The idea was suggested to us that it might be interesting to record what could be done with a group of ambulatory, obese patients who were attending the outpatient department of the Buffalo General Hospital. We placed them on low caloric diets to see whether we could: (1) Accomplish large losses of weight. (2) Determine whether or not certain physiological factors which are ordinarily disturbed in starvation and inanition, would be affected by prolonged dietary restriction.

Our original plan was to place the subjects on the diet suggested by Evans, Strang and McCluggage,[19] but later it was decided that this diet was so limited in variety that no patient could be trusted to follow it accurately except when in a metabolic ward. Therefore we decided to use a somewhat higher caloric diet than the one advocated by them. We did not hope for perfect co-operation nor did we get it from any one. Nevertheless, by seeing patients frequently, by encouraging them and by using a mild bullying attitude toward a few of the less co-operative, we were able to get 32 patients to remain on a restricted diet for from 2 to 17 months. Thirty-one of these patients were women. The report of our studies follows.

A tentative analysis of the etiological factors elicited in the case histories is given in Table 1. It is evident that a multiplicity of such factors usually was present. Such a method of inquiry cannot prove whether or not a tendency to overeat was inherent in the subjects' make-up. Too great an emphasis cannot be laid, therefore, on the small number of cases who showed endogenous factors alone.

TABLE 1
Etiological Factors

Possible Causative Influence	General Incidence	Only Known Cause
Pregnancy	30 cases (65%)	5 cases (11%)
Overeating	31 cases (67%)	5 cases (11%)
Heredity	27 cases (59%)	2 cases (4%)
Surgical procedures	20 cases (43%)	0 cases (0%)
Endocrine disturbances	10 cases (22%)	0 cases (0%)
Menopause	9 cases (20%)	1 case (2%)

Table 2 gives the symptoms most commonly noted. It is evident that some of these are frequently associated with hypertension. To show that high blood pressure is not generally the cause of these symptoms in the obese subjects used in this study, the incidence of each in the hypertensive cases and in the cases with normal blood pressure has been indicated.

TABLE 2
Symptoms and Signs Occurring in the Group of 46

	Patients	With Hypertension	Without Hypertension
Dyspnoea	43 cases (93%)	94%	93%
Fatigue	35 cases (76%)	88%	69%
Dizziness	24 cases (52%)	76%	38%
Edema	33 cases (72%)	75%	62%
Varicose veins	8 cases (17%)		
Backache	9 cases (20%)		
Hypertension	17 cases (37%)		

The *dyspnoea* which occurs in obesity apparently bears no relationship to the hypertension. It is due to a combination of factors. The tendency to dyspnoea in the obese may be accounted for in part by a reduction in vital capacity. Prodger and Dennig[20] showed that in the obese the vital capacities were distinctly below normal—25% below. On the other hand, Bowen[21] concluded that in this affection the vital capacity is but slightly less than normal. Excessive fat in the abdominal cavity may limit materially the freedom of movement of the diaphragm and other organs and so cause this dyspnoea.

The ease with which obese people tire on slight exertion probably is due to the accumulation of fat in, and around, their muscles; such a state may interfere with easy muscle contractility.

Dizziness, which occurred in more than one-half of the cases, is not easy to explain. It was found twice as often in patients with hypertension as in those without. It would seem that the elevation in blood pressure possibly had something to do with its occurrence, as dizziness is a common symptom in hypertension of any type. On the other hand, it occurred in 11 patients who had no hypertension.

Newburgh[6] has called attention to the fact that water retention is of common occurrence in obesity. Wilder, Smith and Sandford,[8] and Rowntree and Brunsting[22] concur. Nevertheless, the presence of visible edema in 72% of our cases was surprising. We thought that it might be due to hypertension but there was so little difference in the incidence of edema in the hypertensive and the non-hypertensive cases that elevated blood pressure probably was not the cause in this group. *Edema* was present in 7 of the 8 cases with varicose veins, suggesting that the varicose veins might be a contributory cause to the edema in these instances. Edema probably is due to the great tendency of obese people to retain water. Possibly also there may be a slight cardiac factor involved in some cases.

We considered any pressure of 150 m.m. or over as *hypertension*. Using this arbitrary figure, we found 17 cases (37%) hypertensive. In Foster's[23] series, 50% had hypertension. It was demonstrated by Rose[24] and also by Bauman[29] that blood pressure drops considerably with weight reduction in obese hypertensives. Rose states that in his series weight reduction is an effective means of reducing high blood pres-

sure but that a period of overeating is likely to cause a rise in the blood pressure to its former point.

Weight reduction is indicated in all cases of simple obesity. It is also beneficial in most cases of hypertension. Often it affords the only means of relief for the backache or footstrain accompanying obesity. In obese cardiac cases, reduction in weight decreases myocardial strain but these cases differ from the uncomplicated obese patients in that the weight must be reduced more slowly (not more than 6 to 8 pounds per month) because cardiac decompensation sometimes is brought about by too rapid reduction in surplus weight.

An extremely obese person is not a good surgical risk, since infection frequently takes place in the fatty tissue-layers after operation and also since postoperative hernia may occur. The majority of gall bladder cases usually are overweight and if surgical intervention is not an emergency procedure these patients will do better when considerable weight is taken off before surgery is undertaken.

The most important factor in reducing the weight of the obese individual is to limit his food intake to such an extent that he has to burn his own fat in order to obtain enough energy to carry on his work.

There are various ideas as to how this should be done. McLester[1] and others think that it should be accomplished gradually by moderate diets. McLester states that the patient should lose between 4 and 5 pounds a month until 25 pounds have been taken from his weight. Then the diet should be increased so that the patient maintains the original loss for 3 to 4 months. The difficulty with this plan is that the progress of treatment is so long and the tangible results so slow that the majority of patients lose interest, become discouraged and stop treatment entirely.

Evans, Strang and McCluggage[19] go to the opposite extreme. They give diets of 400 to 600 calories and say that patients can be kept on them for months with rapid weight loss and nothing but improvement in their general condition. Acidosis does not result except possibly for the first few days. These clinicians use 60 grams of protein, 40 grams of carbohydrate and as little fat as possible, preferably not over 11 grams. With regimen thus determined, 187 of their patients dieted for an average of 8.7 weeks and lost an average of 30.5 pounds, *i.e.* approximately 3.5 pounds a week. A variety of obscure symptoms and minor ailments disappeared. Very few patients complained of hunger and all mentioned an increase in their resistance to fatigue and a feeling of well-being. The patients were hospitalized and were given viosterol and yeast to maintain vitamin balance.

We did not use Evans' diet in our series of cases for the following reasons: (a) for two weeks, a patient placed on the Evans' diet does not maintain nitrogen equilibrium; (b) The diet was considered too drastic for outpatients who were not under constant observation.

On the other hand, we regarded the McLester diet as too conservative and did not think that we could maintain the interest and co-operation of our patients by this slow process. If Evans and others considered that, over a prolonged period of time, no harm was done to their patients after most careful and frequent examinations of the physical condition and physiological state, we believed that a diet somewhat higher than Evans' and considerably lower than McLester's would be perfectly safe. To be certain of this, we also made frequent physical examinations and periodic basal metabolic determinations and, in addition, chemical studies of the blood and urine for those substances which are disturbed in starvation or long continued inanition.

DIET PRESCRIBED: We used a diet of 40 grams of carbohydrate, 85 grams of protein, and 40 grams of fat; this diet is well balanced and should not, and did not, produce a ketosis. It was somewhat inadequate in vitamin A and D and we watched our patients carefully for any disturbance from such deficiency. In constructing the diet, the satiety value of foods was considered; we made use of those foods which have great satisfying effect, such as meat, clear meat broths with the fat well removed, eggs, green vegetables and cheese.

The diet carefully was explained to the patients and they were told the importance of co-operation. They were seen at intervals of two weeks when they were weighed and carefully questioned. Our greatest difficulty resulted from the expense of the diet. Out of a total of 46 cases on whom these studies were attempted 32 (70%) followed instructions for two months or longer. The co-operation was not perfect in any single case but, unquestionably, the patients' caloric

TABLE 3

Buffalo General Hospital Outpatient Obesity Diet

CARBOHYDRATE—40 *PROTEIN*—80 *FAT*—40 *CALORIES*—840

Breakfast:

Skimmed milk	½ cup
10% Carbohydrate fruits	½ cup
Eggs	2
Lean meat (broiled ham)	1 serving 3½"x3"x¼"

Lunch and Dinner:

Choice of one	Lean meat	1 serving 6"x3"x¼"
	Fish	1 serving 5½"x1½"x¾"
	Cottage cheese	½ cup
5% Carbohydrate vegetables		¾ cup
10% Carbohydrate fruits		¼ cup
Skimmed milk		¼ cup
Coffee or tea with each meal (no sugar or cream allowed)		

COST OF DIET—$1.57 per week.

intake was a great deal less than it would have been without dietetic restriction. Without a doubt, the results would have been better if the patients had been hospitalized and placed under constant supervision, but this was impossible.

Weight loss. The 32 cases lost a total of 463 pounds in the first 8 weeks, or an average of 1.8 pounds per week, as compared with 3.5 pounds per week lost by Evans' who were hospitalized and were on a much lower caloric intake.

TABLE 4

Loss of Weight in Pounds and Percentages of Loss Compared With Ideal Weight

32 cases who co-operated 2 months or longer.

Case No.	Loss Pounds	% Loss	Time Days	Case No.	Loss Pounds	% Loss	Time Days
1	39	29%	385	17	9	8%	119
2	17	13%	95	18	46	33%	77
3	23	16%	112	19	80	60%	314
4	25	21%	329	20	25	17%	232
5	23	17%	189	21	43	19%	410
6	9	16%	66	22	53	39%	585
7	31	20%	304	23	54	39%	431
8	33½	25%	294	24	24	20%	96
9	21	16%	203	25	28	22%	224
10	37½	27%	371	26	53	40%	260
11	40	31%	189	27	20	14%	150
12	26½	22%	294	28	36	30%	97
13	20	15%	144	29	28	13%	315
14	73	56%	315	30	15	10%	85
15	23	16%	266	31	10	8%	74
16	60½	41%	504	32	22	17%	83

As shown in Table 4, thirty-two patients remained on the diet for 2 months or longer, the entire group averaging 34 weeks. The 32 lost 1,048 pounds, an average of 0.96 pounds per week. According to the height-weight tables compiled by C. B. Davenport,[25] the group averaged 63.3% over the ideal weight before dietetic restriction was instituted, as against 39.5% over the ideal weight after 34 weeks of dietary treatment: a loss of 24.1%. Since these figures were compiled, two patients have reached their ideal weights.

TABLE 5

Results of Treatment on Symptoms and Signs in the 32 Cases Under Treatment for 2 Months or Longer.

Symptom	Originally Present	Cured	Improved	Not Improved
Dyspnoea	30 (94%)	8 (26.7%)	19 (63.3%)	3 (10%)
Easy fatigue	26 (81%)	8 (30.8%)	15 (57.7%)	3 (11.5%)
Edema	24 (75%)	7 (29.2%)	13 (54.2%)	4 (16.6%)
Dizziness	19 (59%)	4 (21%)	10 (52.6%)	5 (26.4%)

The symptoms, as indicated in Table 5, distinctly were relieved under treatment, with the possible exception of dizziness. Dyspnoea usually was the first symptom which lessened with weight reduction, the improvement often being noted after the loss of the first 10 to 15 pounds. Easy fatigue generally was the next to respond, as evidenced by the fact that the patients suffering from it were able to do more work. Edema subsided in the majority of cases, but tended to recur.

Endocrine disease was diagnosed with great hesitancy. Harrop states that unless an endocrine diagnosis is quite clearly defined, it should not be made. In the great majority of cases the therapeutic problem primarily is that of simple obesity. Two of our cases were diagnosed "hypopituitarism" because of their physical appearances, the bizarre glucose tolerance test, and the small *sella turcica* as demonstrated by X-ray. Three "ovarian" cases were diagnosed because either they had had both ovaries or parts of both ovaries removed surgically, with the resultant artificial menopause, or had marked lessening of the menstrual flow. Two cases were diagnosed "hypothyroidism" because of their symptoms, physical signs and lowered basal metabolic rates. Neither of these cases was given thyroid extract and neither co-operated on his diet over any period of time. Three cases were considered in the endocrine group though no definite diagnosis of hypothyroidism could be made because of normal basal metabolism. Nevertheless, they gained considerable weight following subtotal thyroidectomies for toxic thyroid. They were referred by the thyroid clinic to have their weights reduced.

The ten "endocrine" cases lost an average of 1.2 pounds per week, which compared very well with the cases of simple obesity. The three post-thyroidectomy cases lost weight much more rapidly than did any other group. They lost an average of 2.9 pounds per week for a period of 11 weeks, and even after this, they continued their weight loss at an unusually rapid rate. We are unable to explain this on any other basis than that of disturbed water balance.

Retention of water plays a great part in weight fluctuations and should be borne in mind in the treatment of obesity. It was not uncommon, in this series of cases, to see patients lose from 8 to 12 pounds during the first two weeks on the diet while the weight of others remained stationary or even increased during this period.

The most common causes of water retention are congestive heart failure, lowered blood protein and sodium chloride retention. Physical examination ruled out gross heart failure as a cause in all of our cases. The total protein percentage in the blood, (which was determined routinely), eliminated protein deficiency as an etiological factor. This left sodium chloride retention, which is difficult to demonstrate, as a possible cause. In many cases we reduced the sodium chloride intake to a *minimum without significant results.*

In some cases with unquestionable water retention, we thought that it would be interesting and desirable to see if we could use some therapeutic means of combating it. Wohl[27] used *salyrgan* in some of his obese cases. Potassium chloride was used by us in 4 cases which had obstinate edema as a result of water retention. It was given in varying doses and was administered according to the method of Barker[28] by putting the total amount to be used for 24 hours in a salt shaker and using it instead of ordinary table salt which was omitted in these cases. What was left in the salt shaker after the last meal was put into a glass and diluted with water and taken in this way.

One patient, taking 4 grams per day, lost 6 pounds in 2 weeks. A fairly marked diuresis occurred. There was a diminution in the edema. Another patient lost 9 pounds in 5 weeks with a loss of the edema. The other 2 cases are reported in Tables 6 and 7.

Both patients showed evidences of edema when they first presented themselves at the Clinic. Both showed marked losses of weight during the earlier stages of treatment, followed by a period when the weight practically was constant. In both, further loss occurred when the diuretic was given, and both also lost weight later without the use of the diuretic. One patient (F. G.) reported noting a marked diuresis during the time when the water was given up by the tissues. The other (S. J.) was given large amounts of water during one period and showed a coincident gain in weight, illustrating the mechanism which we believe sometimes obscures the effect of the diet.

TABLE 6

Patient F. G.—Water Retention Case

Date	CHO	Pro.	Fat	Weight	Medication	Clinical Observations
4/ 1/33	115	70	50	262	None	Edema of legs marked
4/28/33	40	80	45	248	None	
7/28/33	40	80	45	225	None	
9/22/33	40	80	45	203	None	
10/ 6/33	40	80	45	201	None	
10/13/33	40	80	45	207	None	Legs considerably swollen
10/20/33	40	80	45	203	None	Legs swollen—feels weak
10/27/33	40	80	45	205	KCL—4 gms. per day	
11/ 3/33	40	80	45	200	KCL—4 gms. alternate days	Nauseated—so took KCL on alternate days
11/17/33	40	80	45	193	KCL—4 gms. alternate days	Urinates 9-10 times a day. Edema much better
12/ 1/33	40	80	45	195	KCL—4 gms. alternate days	Overeating—swelling of legs increased
12/15/33	40	80	45	189	KCL—4 gms. alternate days	
1/ 5/34	40	80	45	190	None	Overeating—legs moderately swollen
2/ 2/34	40	80	45	182	None	
2/16/34	40	80	45	177	None	Feels better in all ways. Edema disappeared

TABLE 7

Patient S. J.—Water Retention Case

CARBOHYDRATE—40 gms. *PROTEIN*—80 gms. *FAT*—40 gms.

Date	Weight	Medication	Clinical Observations
3/10/33	264	None	Edema of legs present
4/28/33	241	None	
6/23/33	225	None	
8/ 1/33	217	None	Edema still present but better
8/18/33	208	None	Edema much better
9/ 1/33	205	None	Edema much better
9/15/33	210	KCL—4 gms. per day	Edema more marked. Omit salt from diet.
9/20/33	200	KCL—4 gms. daily	Edema improved
9/29/33	197	KCL—4 gms. daily	Edema almost disappeared
10/13/33	199	Omit KCL—Take 5 qts. water daily	Overate. Edema not present
10/20/33	206	Omit water. No KCL	Dyspnoeic, weak. Edema of legs again present
11/10/33	200	None	Felt well
11/24/33	196	None	Felt well. No edema
2/16/34	190½	KCL—4 gms. daily	Noticed edema of legs for past few weeks.

Outside of the common complaint that many of the patients felt "cold" more frequently than before they started to lose weight, with one possible exception, there were no complications. This patient developed a large number of cavities in her teeth. This was unusual for her because she had had frequent dental examinations previously and had developed cavities only on rare occasions. The diet which we used was moderately low in vitamin A and vitamin D, a fact which we appreciated, and on account of which we had watched carefully for any signs of deficiency. This was the only patient who showed any possible result of such a shortcoming.

Results of laboratory tests. The patients whose treatment is discussed were studied by various laboratory methods. The object of these studies was three-fold: (1) to detect abnormalities in the group or in single patients which variations should be taken into consideration in planning the method of treatment; (2) to find out whether any changes developed during treatment which would indicate that the therapeutic regimen should be modified; (3) to investigate the effects of prolonged, slight dietary deficiency or undernutrition upon certain chemical and physiological conditions in human subjects.

The factors chosen for study were such as are known to vary in acute starvation. They were: the concentration of uric acid and cholesterol in the blood, of albumin and globulin in the serum, the excretion of creatine in the urine, the basal metabolism, and the effect of the ingestion of 100 grams of glucose upon the venous blood sugar. Uric acid was determined by the direct method of Folin,[30] cholesterol by that of Bloor,[31] albumin and globulin according to the micro-modification of the method of Howe[32] described by Hubbard and Sly,[33] urine-creatine by the micro-technique of Folin,[34] the basal metabolism by the use of the Benedict, portable respiration calorimeter[35] (Sanborn type) and the blood sugar before and after the administration of glucose by Myers' and Bailey's[36] modification of the Lewis-Benedict[37] picric acid method.

TABLE 8

Average Values by Determinations
Determinations before diet

Analysis	Number	Results
Uric Acid	44 tests	1.18 mg. per 100 c.c. blood
Cholesterol	42 tests	158 mg. per 100 c.c. blood
Albumin	16 tests	4.78 gm. per 100 c.c. serum
Globulin	16 tests	2.67 gm. per 100 c.c. serum
Urine creatinine	31 tests	11.9 per cent of total creatinine
Basal metabolism	55 tests	+3.9 per cent deviation from normal
Glucose tolerance	52 tests	
(before glucose)		122 mg. per 100 c.c. blood
(0.5 hrs. after glucose)		168 mg. per 100 c.c. blood
(1 hr. after glucose)		181 mg. per 100 c.c. blood
(2 hrs. after glucose)		145 mg. per 100 c.c. blood
Urea nitrogen	26 tests	11.7 mg. per 100 c.c. blood
Non-protein nitrogen	37 tests	20.1 mg. per 100 c.c. serum

The averages of the results *before treatment* are given in Table 8. It is evident that all of these returns, except possibly the creatine excretion and the level of blood sugar found in the glucose tolerance test, were well within normal limits. It is perhaps worth noting that the average of the basal metabolism estimations was slightly above the mean normal, for in a group of obese subjects it might be expected that the results would be slightly below that mean.

Satisfactory evaluation of the meaning of the glucose tolerance and of the urine creatine figures is difficult. The starvation, blood sugar values certainly should be considered normal by the method used, and the values after the sugar was given seemed to be inside the normal limits of the test, but to lie toward the upper limit of that normal (see foot note). The determination of creatine was unsatisfactory because it was not possible to obtain specimens of urine which represented twenty-four hour periods, and it was necessary therefore to express the excretion of the compound, not in absolute units, but as the ratio between the amount of creatine and creatinine present in the sample submitted for analysis. Since it is known that adult women, (who formed the great majority of the patients studied), not infrequently excrete creatine from physiological causes,[39] it is evident that the presence of that compound is not necessarily a sign of any unusual metabolic condition.

Table 8 shows, therefore, that the average obese patient does not differ significantly from the normal subject. To determine to what extent individual patients differed from the normal, *distribution tables* of separate values were constructed and studied. These did not suggest conclusions essentially different from those indicated by the average figures, therefore they have been omitted. There was a small number with findings which were somewhat abnormal, but such findings quite frequently are present in any group of patients; it was felt that no particular significance was associated with the results. Perhaps it is worth noting that only 4 of 55 patients showed basal metabolism values which were more than 10% below the mean normal, and, in view of the discussion of water retention given above, that only one had a serum albumin concentration below 4.1%. Perhaps as many as one-fourth of the patients showed blood sugar values after the ingestion of glucose which some investigators might consider abnormal.[40] While these data may indicate the presence in the group of an unusually large number of subjects in the pre-diabetic state[41] or of patients suffering from pituitary disorders,[42] our feeling is that conclusions conservatively should be drawn from the figures and that final diagnosis of metabolic disorders should not rest upon the results of glucose tolerance tests alone.[43]

An attempt was made to repeat these studies at fairly frequent intervals upon the patients who co-operated in the dietetic treatment. In general, these results did not differ noticeably from those obtained when the patients first were seen. There were more urine specimens which apparently contained fairly large amounts of creatine, but we were not able to make out that there was any relationship between this finding and any clinical condition of the patients. Since broth was allowed as an auxiliary dietary factor this may have served as a source of creatine in some instances.[44] There were 3 albumin concentrations below 4.1%, but all were over 3.6%, and therefore above the level which is associated with edema.[45] Results of 8 metabolic tests were 9% or more below the normal mean. None of these figures appeared to indicate conditions which were of any clinical importance. Tables showing these findings are omitted.

TABLE 9

Summary of Results of Last Study Made on Each Patient

Factor Studied	Number of Patients	Days on Diet	AVERAGE VALUES Before Diet	With Diet	Percent Change
Blood uric acid	14	146	4.29 mg.	4.12 mg.	— 4%
Blood cholesterol	13	172	155 mg.	159 mg.	+ 3%
Serum albumin	16	166	4.77 gm.	4.67 gm.	— 2%
Serum globulin	16	166	2.52 gm.	2.47 gm.	— 2%
Urine creatine	13	157	11.4%	15.4%	+35%
Basal metabolism	17	186	4.5%	—2.7%	— 7%
Glucose tolerance	16	180			
before glucose			119 mg.	119 mg.	± 0%
0.5 hrs. after glucose			179 mg.	163 mg.	— 9%
1 hr. after glucose			162 mg.	153 mg.	— 6%
2 hrs. after glucose			135 mg.	140 mg.	+ 4%

In addition to these studies of *individual* patients, which were primarily designed to detect injurious effects of the diet, many tables were constructed in an effort to determine whether there was any effect whatever of the diet upon the factors studied. It is fully recognized that such studies by themselves are of little scientific value for a number of self evident reasons: for example, the relatively small number of patients studied and the incomplete manner in which the diet could be controlled. At the same time, it does seem worth while to present the data, because it may make possible the extension of conclusions drawn from more carefully controlled experiments, such as can be carried out only in organized metabolic wards. In Table 9, the *averages* of the last values obtained are contrasted with the ones found when the same patients first presented themselves at the Clinic. It shows that only the urinary creatine was significantly affected by the diet but that there was some slight change produced in the response to the glucose meal and in the basal metabolic rate.

The reasons why the results of the creatine study cannot be emphasized already have been indicated. They include the unsatisfactory nature of the method used for determining the compound, the excretion of creatine in varying amounts by normal women under various physiological conditions, the presence in the control series before the diet was started of a fairly large number of cases of creatinuria, the possible derivation of creatine from the broth which some patients

The results have been compared with such tables of studies of the glucose tolerance test as are readily accessible. Since most of the figures recently published have been based upon different technical methods from those used in this work, since the amounts of sugar ingested in different investigations have often varied markedly from those used by us and since, in many instances, *capillary* rather than *venous* blood has been used for study, comparisons are difficult.[37] For an extended discussion of this subject see pp. 114-129 and 156-161, Peters and Van Slyke. (*loc. cit.*).

ingested while they were on the diet and, also, the fact, which is not brought out by the table, that the amount of creatine in the urine sometimes decreased when the diet was fed. In spite of these valid criticisms of their significance, it seems worth while calling attention to the results. They were the *only clearly positive finding*. An increase in the degree of creatinuria seems to be the only way in which these patients, who were losing weight quite rapidly at the time of the observations, resembled subjects who are abstaining from food completely. It is well known that creatinuria is increased during fasting periods,[46] and frequently this is an index of unusual tissue destruction,[47] but perhaps it is not generally recognized that it is quite as delicate a sign of this condition as the results given seem to indicate. The authors feel that confirmation of these findings with similar diets, fed under carefully controlled conditions, might justify some interesting speculations.

It has been stated[48] that the basal metabolic rate tends to decrease in under-nutrition and the figures given are in accord with this fact. On the other hand, changes of the order of magnitude shown in the Table probably are little, if any, greater than are frequently noted as patients adapt themselves to the conditions of the test; therefore, the differences must be interpreted rather conservatively.

The changes in the results of the *glucose tolerance* test are interesting. It is known that after a complete fast[49] or following a diet causing ketosis[50] there is an apparent decrease in the tolerance for glucose, with a production of relatively high blood sugar values after the ingestion of that sugar. In our experiments, on the contrary, there was an apparent improvement in tolerance. This would appear to show that the diet did not approximate starvation in at least some of its metabolic effects, but resembled instead simple relative under-nutrition, such as is used sometimes in the treatment of mild diabetes. It is known that such treatment produces changes in the glucose tolerance test similar to those found here.[51]

To determine rather more definitely whether the changes produced by the diet were as nearly negative as Table 9 indicates, more complicated studies utilizing all of the figures obtained while the patients were on the diet were prepared. These showed clearly that no change was produced in the *blood uric acid*. The diet, therefore, did not affect this substance as does complete starvation[52] or the ingestion of severe ketogenic diets,[53] which cause an increase in the concentration of uric acid in the blood. There was likewise no change in the serum globulin—a finding which was not unexpected,[54] although the long period of under-nutrition might conceivably have had some influence upon this blood protein. A very slight decrease in serum albumin may have taken place.[54] The presence of such a decrease was by no means established with certainty by the figures, for the range of the variation was within the limits of error of the methods of the investigation. The figures do make it impossible to state that no change whatever was caused by the diet. Perhaps there was an increase in cholesterol of approximately the same magnitude,[55] and the authors are not justified in concluding that no change in the cholesterol content of the blood resulted from the use of the diet. The more extensive and detailed analyses confirmed the impression of changes in urine creatine, basal metabolism and glucose tolerance shown by Table 9.

The results of these studies indicated that untreated obese patients showed nothing specific in the physiological factors studied unless it was a slightly greater tendency to excrete creatine than is shown by normal women and a somewhat greater increase in the blood sugar, after the administration of glucose, than usually is found in normal subjects. There were no changes induced by the diet which could be considered harmful to the patients. The degree of creatinuria appeared to increase somewhat and there was a slight decrease in the basal metabolism. The tolerance for glucose was somewhat improved by the diet. The results indicated that no change in the level of uric acid in the blood or of globulin in the serum was produced. While it cannot be said that no evidences of change in the blood cholesterol or in the serum albumin were obtained, it can be stated that the changes were very slight and that the evidence of their presence was unsatisfactory.

CONCLUSIONS

A study of a group of obese patients presenting themselves at an outpatient department convinced us that obesity is a syndrome which has the following symptoms and signs: dyspnoea, easy fatigue, edema, dizziness and hypertension.

In 71% of these patients multiple factors, both endogenous and exogenous, seemed to play some part in the etiology. Twenty percent were considered endocrine in origin.

Results of chemical and metabolic studies of the patients did not differ significantly from those obtained on normal subjects.

A diet of 680 calories was prescribed. It was found, that by sympathetic understanding and persuasion on the part of the physician, patients could be carried over the first 2 to 4 weeks of dieting, after which their desires for food lessened. Three quarters of the group co-operated quite closely for periods of from 2 to 17 months.

By this regimen patients lost an average of 0.96 pounds per week. Patients classified in the endocrine group lost weight at about the same rate as did the others; it is worthy of note that 3 patients upon whom thyroidectomies had been performed lost three times as rapidly as did the average.

In general the rate of weight loss was twice as fast during the first 8 weeks of treatment as it was subsequently. A part of this difference in rate seemed to be due to water retention, which at times was so great as to lead to the development of visible edema. This could be relieved in some instances by the oral administration of potassium chloride.

No significant physiological changes were produced by the diet, and such changes as were noted were quite different from those found in complete starvation.

The symptoms, with the exception of dizziness, were cured or improved in approximately 90% of the cases.

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THE INCIDENCE AND SIGNIFICANCE OF DISEASE OF THE GALL BLADDER AND LIVER IN PERNICIOUS ANEMIA*

By

FRANK H. BETHELL, M.D.
ANN ARBOR, MICHIGAN

and

BERNARD D. HARRINGTON, M.D.
INDIANAPOLIS, INDIANA

IN PERNICIOUS anemia the frequent occurrence of symptoms referable to the digestive tract impressed the earliest observers of this condition. Later, the almost universal finding of achlorhydria in pernicious anemia with the appearance of bacteria high up in the gastro-intestinal tract suggested intestinal sepsis as its direct cause.[1] Recent studies have tended to replace this view with the consideration of pernicious anemia as an intrinsic deficiency disease, the digestive symptoms being due primarily to the anemia, but also in part to disordered gastric digestion, and in part to atony, the consequence of spinal cord involvement.[2] However, that there is in pernicious anemia an increase in the intestinal flora, and that bacteria, particularly *B. Coli, streptococci,* and *B. welchii,* are present at abnormally high levels of the digestive tract has been amply demonstrated by many investigators.[3, 4, 5] Davidson and Gulland make the statement, "there appears to be no doubt that the achlorhydria is responsible for the gastro-intestinal sepsis which is found in every case of pernicious anemia."[6]

The existence of abnormally large numbers of potentially pathogenic bacteria in the upper digestive tract does not denote active infection, but it is quite possible that disease of bacterial origin is of increased frequency in individuals harboring excessive numbers of such organisms. While infection is no longer generally held to be the primary cause of pernicious anemia, it cannot be denied that its presence

*From the Thomas Henry Simpson Memorial Institute for Medical Research, and the Department of Roentgenology of the University Hospital, University of Michigan, Ann Arbor, Michigan.
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may modify the course of the disease and impair the efficacy of its treatment.[7, 8, 9]

The location of the orifice of the common bile duct renders the biliary tract, and more especially the gall bladder, particularly suitable for an evaluation of the relationship between upper intestinal sepsis and the incidence of infection. The question of the mode of entrance of organisms to the gall bladder, whether by the blood stream or by ascent of the common bile duct, does not concern us here since, in the great majority of cases of cholecystitis, the primary source of infection is the digestive tract, although the route may be hematogenous. A number of observers have commented on the apparent frequency of cholecystitis accompanying pernicious anemia.[6, 10, 11, 12, 13, 14] Such reports for the most part antedate the present concepts of pernicious anemia and were made usually in an attempt to establish an etiological relationship between the two conditions. In many of the cases described, positive evidence of gall bladder pathology sufficient to cause functional derangement is lacking. Consequently, in the light of our present knowledge, a further consideration of the question seems justifiable.

MATERIAL STUDIED

Employed for this purpose, were fifty-eight patients seen at the Simpson Memorial Institute and demonstrated to have pernicious anemia by clinical criteria, blood examination and response to specific therapy. For the most part, the cases were taken consecutively and no attempt at selection was made. In all of these patients, achlorhydria was found by fractional gastric analysis after subcutaneous injection of histamine hydrochloride. There were 34 (59%) males and 24 (41%) females in the series. The age limits were 21 and 73 years, but 90% of the patients were between 40 and 70 years old. The majority of the patients had had their disease longer than three years.

Evidence of biliary tract disease was secured by symptomatology, physical findings and cholecystography. Estimation of liver function was attempted by quantitative serum bilirubin determination, by the rate of absorption of the dye, phenol-tetraiod-phthalein sodium ("iso-iodeikon") from the blood stream and, in a few cases, by the galactose tolerance test.

Fifty-three (91%) of the members of this group complained of some form of digestive disturbance other than soreness of the tongue or simple anorexia. Constipation was most common, 40 patients (68%) complaining of this symptom. Thirty-two (55%) complained of nausea with vomiting and the same number of abdominal discomfort with distention; the latter usually was referred to as "dyspepsia." Nineteen (32%) had diarrhoea, commonly alternating with constipation. Seven (12%) suffered with upper abdominal pain, generalized, moderately severe, and bearing no apparent relation to meals. Four (7%) gave a history of transient jaundice other than that associated with severe anemia.

Of the 53 patients complaining of digestive disorders, 31 (53%) experienced complete relief from such symptoms after remission induced by anti-anemic therapy; 22 (38%) were improved, and 5 (9%) were unimproved.

Physical examination revealed no signs referable to the digestive tract in 26 (50%) members of the series. Enlargement of the liver, slight or moderate in degree, was present in 31 (53%) and tenderness in the gall bladder area was elicited by palpation in 11 (19%) of the patients.

Cholecystography was done after intravenous administration of phenol-tetraiod-phthalein sodium ("iso-iodeikon"); .04 gm. of the dye were injected for each kilogram of body weight with a maximum of 2.5 gm. The dye was dissolved in 50 c.c. of sterile redistilled water, filtered, sterilized in a boiling water bath for fifteen minutes, mixed with 200 c.c. of sterile physiologic salt solution, and administered by gravity, usually into the median basilic vein. The passage of the dye was preceded and followed by the injection of a few cubic centimeters of physiologic salt solution. The rate of injection varied between 8 and 12 c.c. a minute. *Reactions* were fairly frequent. Of the 58 cases 21 (36%) suffered chills and transient pyrexia, the former occurring, as a rule, about one hour after the beginning of the injection. Two cases developed generalized urticaria commencing a few hours after the administration of the dye and lasting about 24 hours. There were several cases of endophlebitis following the injection, although extravasation of the dye or injecting it into the wall of the vein could, with reasonable certainty, be excluded. In none of the patients were the symptoms induced by the dye of an alarming nature.

Roentgenograms were made of the gall bladder area at four- and eight-hour intervals after commencing the injection of the dye. The response to fat was determined by the administration of 120 c.c. of 40% cream after the eight hour films, followed in one hour by a final exposure. At the beginning of the study, roentgenograms were taken before the administration of the dye, but as this procedure apparently yielded no useful information, it was discontinued.

By roentgenological criteria abnormal gall bladder function was present in 13 of the 58 cases (22.5%). In 9, there was non-visualization of the gall bladder. In three cases, cholelithiasis was found. Of the 4 cases of dysfunction with visualization stones were seen in 2. The others possessed large, faintly-filling gall bladders without evidence of concentration of the dye after ingestion of fat.

The rate of absorption of the dye from the blood stream was determined by removing samples of venous blood at 30 and 60 minute intervals, following the injection of the dye solution, and estimating the concentration of the dye in the serum according to the method of Cole, Copher, and Graham.[15] In the series of standards used for comparison, 100% is assumed to represent the concentration of the dye in the plasma immediately after injection and diffusion through the blood stream. Several samples, on different individuals taken at this time, were found to have a value of approximately 100%. It is, of course, recognized that the validity of this test depends upon a constant plasma-volume relative to the amount of dye injected. In pernicious anemia in relapse, there is a marked reduction in total blood-volume, the absolute plasma volume, however, undergoes but little change from the normal, although in some cases it is slightly increased.[16] Moreover, the cases comprising the present study were not subjected to cholecystography until after response to anti-anemic therapy clearly had been evidenced. The upper limit of normal dye retention was considered to be 15% in the 30 minute specimen and 10% in the 60 minute specimen.

Forty cases (69%) fell into the normal group; their average dye retention at the 30 minute period was 10.4%, at the 60 minute period it was 5.1%. In 18 (31%) of the patients studied, there was delayed absorption of the dye; the average retention at 30 minutes was 39.5%, at 60 minutes it was 17.8%. The delayed dye absorption in these cases may be accounted for by injury to the liver cells, dependent upon deficient oxygenation, a condition described by Rich and Resnik.[17]

Quantitative serum bilirubin estimations were made at weekly intervals on 49 of the patients while under observa-

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tion in the hospital. The bilirubin content of the serum is, of course, elevated during pernicious anemia in relapse, and, consequently, in these cases, samples considered significant were taken after adequate response to anti-anemic therapy had occurred, but even with such precautions, high values as an indication of liver dysfunction are open to question. In 39 cases (79.5%) the bilirubin value was less than 0.75 mgm. per 100 c.c. In 10 cases (20.5%) whose readings were above 0.75 mgm. per 100 c.c. the average value was 1.0 mgm.

A galactose tolerance test, consisting of the ingestion of 40 gm. of galactose and the subsequent estimation of the blood and urine sugar at hourly intervals for 3 hours, was found to be negative in the few instances in which it was done.

The clinical and laboratory data obtained from this series of cases of pernicious anemia provide certain interesting correlations. Of 13 patients presenting roentgenological evidence of gall bladder dysfunction, 12 had gastro-intestinal symptoms present during relapse other than anorexia and constipation; in 10 instances the symptoms persisted after remission of the anemia had been induced. Of the 15 patients in whom X-ray findings were negative, 8 complained of persistence of gastro-intestinal symptoms. There is no apparent relationship between instances of gall bladder dysfunction and abnormal liver function as tested by the rate of absorption of "iso-iodeikon" from the blood stream, but it is perhaps worthy of note that, of 21 patients who had chills following intravenous administration of "iso-iodeikon," 16 had delayed absorption of the dye from the blood stream. Only 2 of 37 patients who did *not* have chills showed delayed absorption of the dye.

The patients under consideration were, for the most part, treated with liver extract by intravenous injection. The usual maintenance-dose after remission had been induced was one injection of 20 c.c. every 4 weeks, representing the extract derived from 100 gms. of fresh liver. Of the negative gall bladder group of 45 cases, 40 were observed for from 3 months to 2 years after remission. The average red blood cell count among the males was 4,650,000 per cu. mm.; among the females 4,520,000 per cu. mm. during this period of observation. Of the 13 cases whose cholecystographic studies revealed dysfunction, one died of empyema of the gall bladder and septicemia; 8 were followed over a considerable period of time. The average blood counts and treatment administered during this interval are given for each patient.

Name	Sex	Average Red Blood Cell Count	Treatment
O.B.	M	4,620,000 per Cu. mm.	Intrav. Liver Ext. 20 c.c. every 4 weeks.
E.E.	M	4,410,000 " " "	" " " " " " " "
C.S.	M	4,410,000 " " "	" " " " " " " "
C.B.	M	3,740,000 " " "	" " " " " " 2 "
C.S.	F	3,530,000 " " "	" " " " " " 3 "
A.Y.	F	3,990,000 " " "	" " " " " " " "
A.B.	F	4,400,000 " " "	" " " " " " 4 "
E.S.	F	4,000,000 " " "	Liver Ext. No. 343. 6 vials daily.

The average red blood cell count of the males in this group was 4,300,000 per cu. mm.; of the females 3,980,000 per cu. mm., values appreciably lower than those obtained from the "negative" members of the series. It should also be noted that 4 of these patients received treatment considerably in excess of that usually required for maintenance. It is recognized that conditions other than disease of the gall bladder, such as infection elsewhere or arteriosclerosis, could have influenced the response of these patients to anti-anemic therapy: but such factors were no more prevalent in this group than in the larger series of patients with normal gall bladder function.

There is apparently no association between the response to specific treatment and the function of the liver as tested by the serum bilirubin value and the rate of dye absorption.

CONCLUSIONS

Clinical and roentgenological evidence of a rather high incidence of gall bladder disease in pernicious anemia is presented. Intravenous cholecystography performed on 58 patients, revealed gall bladder dysfunction in 13 (22.5%). The roentgenologic impression was supported by clinical criteria in 10 of these 13 patients.

Although 31% of the patients studied showed delayed absorption from the blood stream of the dye, phenol-tetraiodophthalein sodium, the presence of impaired liver function was not confirmed by clinical findings or by the subsequent course of the patients' illnesses.

There was an apparent association between delayed absorption of the dye and reactions, characterized by chills and fever, following its injection.

Persistence of gastro-intestinal symptoms in persons suffering with pernicious anemia, after remission has been induced, strongly suggests the presence of gall bladder disease.

In pernicious anemia chronic disease of the gall bladder may modify seriously the expected response to anti-anemic therapy.

ABSTRACTS

DUNCAN, GARFIELD G. AND FETTER, FERDINAND.,
The Effect of Pregnancy on the Insulin Requirement of the Diabetic. P. 347-351.

There are conflicting views regarding the effect of pregnancy on the insulin requirement of the diabetic. This is due largely to the infrequency of pregnancy in the diabetics who require insulin. Seventy-eight pregnancies complicating diabetes were collected from the literature to which are added the six reported in this paper. The diabetic's tolerance during pregnancy was impaired in 55.9% of the cases. Tolerance was unchanged in 19.1% and in 25% was improved. The authors conclude that pregnancies under ideal conditions and treatment does not permanently impair the diabetic's tolerance and that diabetes *per se* is not a contraindication to pregnancy.

William Gerry Morgan and William M. Ballinger.

COLLENS, WILLIAM S.
One Hundred Obesity Diets on One Chart. P. 683-687.

Collens presents a chart devised to make available for direct reading and without any calculations whatsoever, one hundred diets for cases of obesity. The diets range from 600 to 1,400 calories per day.

William Gerry Morgan and William M. Ballinger.

RINEHART, J. F. AND METTIER, S. R.
The Heart Valves and Muscle in Experimental Scurvy with Superimposed Infection—With notes on the similarity of the Lesions to those of rheumatic fever. The Amer. Jour. Path., X, 1:61-80, January, 1934.

Experiments were conducted upon guinea pigs directed to the determination of the effect upon the heart valves and muscle of: 1. uncomplicated scurvy, acute and chronic; 2. scurvy combined with infection, and; 3. infection alone.

The animals were placed upon a basic diet deficient only in Vitamin C. To the diet of the control animals and of those receiving inoculations of a beta-streptococcus, orange juice was added to make up this deficiency.

The study led to the following observations: Infection in animals maintained on an adequate diet usually produces no significant lesions in the heart valves. When present, they are exudative rather than proliferative in type. In uncomplicated scurvy definite atrophic and degenerative changes occur in the collagenous stroma of the heart valves. In scurvy with added infection lesions of a combined degenerative and proliferative character develop in the heart valves with considerable frequency. These lesions are strikingly similar to those of acute rheumatic fever. They consist of swelling and degeneration in the stroma and a diffuse subendothelial proliferation. Proliferative nodules composed of hyperplastic cells resemble the Aschoff reaction of rheumatic fever. The fibrinoid degeneration described by Klinge, and believed by him to be the fundamental and earliest lesion of rheumatic fever, is observed. Micro-organisms were not observed in a limited number of stained sections studied.

The authors advance the theory that a condition of Vitamin C undernutrition may be a necessary background for the development of rheumatic fever; when the insult of infarction is combined with the scorbutic state, the pathological picture of rheumatic fever develops.

N. W. Jones.

RUFFIN, JULIAN M., AND SMITH, DAVID T.
The Treatment of Pellagra with Certain Preparations of Liver. Am. Jour. Med. Sc., Vol. 187, No. 4, April, 1934.

The authors have discussed close similarity in the symptoms of of pellagra and pernicious anemia of the Addisonian type. They placed the patients on a standard basic diet containing an adequate amount of proteins, fats, carbohydrates, minerals and all the known vitamins excepting vitamin "G" (B_2). The patients did not improve on this diet. The addition of oral administration of an aqueous extract of liver in doses of 90 c.c. daily, effected a cure in ten cases. Five patients on the same basic diet showed little or no improvement when given liver extract intramuscularly in doses of 5 c.c. daily, but substitution of the oral aqueous extract of liver was very effective.

H. W. Soper.

CRIMM, PAUL D. AND STRAYER, J. W.
Vitamin Therapy in Pulmonary Tuberculosis. V. The Effect of Viosterol on the Diffusible and Non-diffusible Calcium of the Blood and Spinal Fluid. P. 557-562.

Their findings are summarized: 1. Viosterol increased the calcium in the blood and spinal fluid of patients with pulmonary tuberdulosis. 2. Viosterol increases both the diffusible and non-diffusible fractions of calcium. The non-diffusible fractions is the more affected. 3. In patients with pulmonary tuberculosis, viosterol reduces the diffusibility ratio by increasing the non-diffusible calcium. In previous work it was observed that a more rapid clearing and fibrosis was evident in some cases of pulmonary tuberculosis after viosterol had been administered. An increase in non-diffusible calcium is present in patients with fibrotic lesions. Therefore these observations lead to the conclusion that an increase in non-diffusible calcium favors the healing of pulmonary tuberculosis.

William Gerry Morgan and William M. Ballinger.

CUSHING, HARVEY.
Hyperactivation of the Neurohypophysis as the Pathological Basis of Eclampsia and other Hypertensive States. The Amer. Jour. of Path. March 1934, Vol. X, No. 2, p. 145.

In a lecture delivered before the Medical Research Society at University College, London, Cushing reviews work reported in the literature and his own studies leading to the belief that hyperactivation of the neurohypophysis, as shown by an infiltration of the basophilic epithelial elements into the posterior lobe of the pituitary body, is the cause of eclampsia and essential hypertension in young persons and possibly also related to atherosclerosis with hypertension in old age. He discusses the frequency of the invading process, the function of the pars intermedia, the role of these invading basophilic elements as activators of the posterior lobe, and he presents data from autopsy studies that suggest a relationship between the degree of invasion and the degree of eclampsia and hypertension present during life.

The presentation is tremendously thought-inspiring, especially to those who have pondered over the frequency of essential hypertension in the young. The author advances the general hypothesis that (1) the source of these hypertensive disorders lies in the posterior lobe of the pituitary body; (2) that the extent of basophilic invasion from the pars intermedia is a measure of posterior lobe activity; and (3) that excessive infiltration by these elements represents the histopathological basis of eclampsia and essential hypertension in young persons and may possibly also be related etiologically to the atherosclerosis of old age.

N. W. Jones.

HENCH, P. S.
The Analgesic Effect of Hepatitis and Jaundice in Chronic Arthritis, Fibrositis and Sciatic Pain. Annals of Int. Med., 7:1278, (April) 1934.

The author summarizes in part as follows: "In the course of the last four years observations have been made on the effect of inter-current intrahepatic jaundice on the chronic pain experienced by 16 patients with chronic arthritis, fibrositis, and sciatica. In two of the cases the intrahepatic jaundice apparently was not related to drugs; in 14 cases it was considered the result of toxic hepatitis caused by cinchophen. Coincident generally with the onset of jaundice, 14 of the 16 patients received partial, or more usually complete, relief of pain for variable periods; moreover, in five of the six cases in which the joints were swollen, reduction of the swelling, sometimes complete, also was noted.

Samuel Morrison.

FRIEDLANDER, RICHARD D.
The Racial Factor in Pernicious Anemia: A Study of Five Hundred Cases. P. 634-642.

Evidence derived from a study of five hundred cases of typical pernicious anemia is presented to confirm the opinion that pernicious anemia is a disease largely confined to the white race in temperate zones and that among these people there is a definite racial, as well as constitutional, pre-disposition, the latter being embodied in individuals endowed with a diathesis characterized by fair complexion, light hair and light-colored eyes.

Wm. Gerry Morgan.
William M. Ballinger.

BRAUNROTH, H. H.
Fluctuation of Sugar Content in Diabetics Produced by Air and Seabaths. Archives f. Verdauungskrankheiten, January, 1934, Vol. 55, No. 1-2.

Diabetics maintain an increased blood sugar level if exposed to bathing in salt waters amounting to about 60 mgm. above normal. Air baths do the same but to a lesser extent, i.e. 30 mgm. According to the severity of diabetes the hyper-glycaemia remains longer, showing even ketonuria at times. It was shown that repeated exposures to baths may influence this tendency in such a way that it may approach conditions as found in healthy individuals.

M. E. Gabor.

MCCLURE, F. J.
A Review of Fluorine and its Physiological Effects. Physiological Review. 13:277-300, July, 1933.

A defect in human teeth known as mottled enamel is endemic in certain parts of the United States, Mexico, and many other countries. This has been attributed to fluorine in the water supply. The mottled enamel is characterized by chalky white patches distributed over the surface and the enamel is often pitted and corroded. The teeth show an absence of translucency, having a dead white glazed appearance. Histologic studies reveal imperfect calcification, particularly of the enamel rods themselves. The intercementing material which is normally present between the enamel rods is lacking. There is experimental evidence indicating that bones may be affected structurally by fluorides.

Dwight Wilbur.

SECTION IV—*Roentgenology*

FACTORS OF ERROR IN ROENTGENOLOGIC DISTINCTION BETWEEN THE NORMAL AND THE DISEASED STOMACH AND DUODENUM

By
B. R. KIRKLIN, M.D.*
ROCHESTER, MINNESOTA

ON THE roentgenologic diagnostician devolves a two-fold duty: to find evidence of disease when disease is present, and to avoid a diagnosis of disease when disease is absent. Of the two duties, the latter is the more difficult to perform. the examiner constantly is tempted to interpret all unusual phenomena in terms of pathologic change. Many factors conduce to such error. Among those which lead to error in gastroduodenal diagnosis are: (1) failure to make due allowance for normal variants or to exclude conditions simulating disease, (2) constant effort to make diagnoses at earlier stages of disease, and hence on more delicate signs, (3) reliance on secondary and indirect phenomena, (4) reliance on a limited roentgenographic examination, (5) prejudice by the mere fact that the patient is *sent* for roentgenologic investigation of the stomach and duodenum, (6) bias from clinical data and (7) desire to corroborate the clinician's opinion.

Current roentgenologic literature deals almost wholly with signs of disease and the distinction of one disease from another. Although textbooks usually devote chapters to the appearance of the normal, its variants and functional alterations and also of conditions simulating disease, these conditions are so numerous and varied that it is almost impossible adequately to describe them. A competent knowledge of the appearance of these normal and abnormal conditions can be gained only by wide experience. Often they mislead the novice in roentgenology or the clinician who is obliged to make his own roentgenologic interpretations.

It is essential, first to comprehend the effect of body build, abdominal tension, and tonus of the gastric musculature on the general form, position, and size of the stomach. Among persons of the *enteroptotic habitus*, whose bodies are long and slender, the stomach is almost invariably hook-shaped and its lower pole is well below the umbilical level. The gastric muscles are more or less hypotonic and, as a result, the stomach is so capacious that dilatation consequent to pyloric obstruction may be suspected to exist. However, in such cases the antral portion of the stomach is not expanded and the pylorus lies near the spinal column, whereas, in cases of dilatation, the antrum is enlarged and the pylorus is displaced to the right. In extreme examples of the *broad habitus*, which are not common, the stomach has the shape of a steer-horn and lies obliquely or almost transversely across the abdomen, high above the umbilical level; it is hypertonic, requires only a moderate amount of opaque medium to fill it completely and is often so narrow that it appears to have been shrunken by a pathologic process.

Ordinarily, the shadow of the barium-filled *normal stomach* has a contour which is regular and smooth, save for indentations produced by peristaltic contractions. The fairly common exceptions to this, however, require note. Not rarely the lesser curvature is indented, sometimes sharply, near the pylorus, and the examiner may ascribe the indentation to organic contraction or else regard the prominence between the indentation and the pyloric ring as the *niche* of an ulcer. Occasionally, marked hypertonus of the *muscularis mucosae* so accentuates the gastric *rugae* that they produce a fine serration along the greater curvature which anomaly might mistakenly be attributed to polyposis.

Although it should be well known that when the transverse colon is distended by gas or fecal material, it is likely to deform the greater curvature of the stomach by pressure, and although the condition should be obvious on the most casual inspection, such deformity often is made the basis for the diagnosis of gastric carcinoma. Sometimes the patient violates the routine instruction to fast before examination, and masses of food which he has taken produce defects similar to those caused by polypoid tumors. Ascites, large abdominal tumors and advanced pregnancy displace the stomach upward and often distort it into the semblance of a viscus extensively diseased.

Although the simulation of gastric lesions by reflex gastrospasm from causes outside the stomach has been warned against for years, the incautious examiner is still sometimes deceived by it. Spastic distortion may take the form of jagged irregularity of the antral borders, a sharp *incisura* in the greater curvature, hour-glass deformity or blurring or obliteration of the prepyloric segment. The so-called "cascade stomach," which has the shape of a retort and in which barium overflows from the expanded cardia into the contracted tubular distal half, is attributable to spasm. Frequently, *gastrospasm* of any variety is transitory or changes in situation or appearance, and thus is recognizable, but it sometimes persists unchanged during the examination. Hence, in any case of gastric deformity which is not accompanied by other roentgenologic manifestations, or by definite physical signs, such as a palpable mass corresponding to the defect, the patient should be given tincture of belladonna to full physiologic effect and be re-examined. Almost invariably the spasm will have disappeared at the second examination.

By *contraction* of the abdominal muscles, the stomach may be pressed upward and distorted into fantastic shapes. Such distortion is seen often among patients who are fearful of the screen examination or of what it may disclose. It is not improbable, also, that many deformities assigned to reflex spasm really are effects of heightened intra-abdominal tension. In all cases the rigidity of the abdominal wall will be apparent during the manipulations which are indispensable to efficient roentgenoscopy, but if these manipulations are omitted the examiner is likely to misinterpret the deformities.

Normal duodenal bulbs vary widely in apparent capacity. Of two bulbs, one may appear to be four times as large as the other, yet both may be quite normal. Hence, the examiner must not assume that a large bulb has been dilated, perhaps as a result of obstruction, or that a small one has been shrunken by disease. Duodenal bulbs also differ considerably in the ratio of length to breadth and in the degree of convexity of their lateral borders. Notwithstanding these variations, the normal bulbar shadow is characterized by its symmetry, homogeneity and its regularity of contour. To elicit these qualities it is essential that the bulb be completely filled with

*Section on Roentgenology, The Mayo Clinic.
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opaque medium. The shadow of an incompletely filled bulb is eccentric, mottled or grossly irregular and the novice is prone to construe it as indicative of duodenal ulcer.

Progress in roentgenologic examination of the alimentary canal has entailed the diagnosis of gastric and duodenal lesions at an earlier stage and hence on slighter evidence than formerly. *A small gastric or duodenal ulcer* unaccompanied by spastic deformity and visible only as a *niche "en face"* exemplifies the type of lesion which the roentgenologist is now expected to discover. To reveal a *niche* of this sort requires that the study be made with only a small amount of barium in the stomach, and that the gastric and duodenal walls be approximated by manual pressure. By such manipulation, however, a small amount of barium may be penned up at the base of the bulb, in the pyloric ring, or in a fold of the gastric rugae and so, be mistaken for a true *niche*. However, a true *niche* is constant in form, size, and in situation, and a gastric *niche* usually is in the midst of converging *rugae* or, if the ulcer is malignant, it is surrounded by an elevated margin.

During the developmental stage of gastroduodenal roentgenology, the secondary phenomena incident to organic disease were strongly emphasized. Changes in gastric capacity, mobility, flexibility, peristalsis and motility, and the spasm produced by intrinsic lesions, were looked for with especial care and given prominence among diagnostic signs. At that time, a high esteem for indirect manifestations was warranted, for technics were imperfect and it was difficult to reveal or to interpret the deformities which directly depicted the lesions themselves. On the other hand, the secondary manifestations were strikingly evident and, in conjunction with clinical data, could be woven into complexes which were often diagnostic. It is true that a gastric residue from the six-hour meal often is most significant of a gastric or duodenal lesion, that peristalsis is likely to be absent in a diseased portion of the gastric wall and that gastrospasm is often associated with lesions of the stomach or duodenum. But there are many exceptions. Patients who suffer attacks of migraine or who take additional food or fluids after the opaque meal are almost certain to have six-hour gastric residues, or such may occur without assignable cause. Peristalsis in normal stomachs is often so sluggish that it cannot be traced throughout, and it is usually absent from spastically deformed segments. The importance of the *incisura* as a sign of gastric ulcer or carcinoma has been overestimated in the past, for its association with these lesions is rare. Occasionally, a gastric *incisura* is associated with duodenal ulcer, but more often, like other forms of gastrospasm, it arises from causes outside the stomach and duodenum. Indirect signs are not valueless, for usually they stimulate search for a causative lesion, occasionally give needed support to direct signs which are hard to discern, and sometimes assist in distinguishing between lesions, but neither singly nor in combination are they sufficient bases for diagnosis.

For the reasons stated, an examination which is solely roentgenographic and limited to a few films is almost never conclusive. When roentgenoscopic equipment is lacking, simple roentgenography is sometimes warranted and may definitely reveal extensive disease, but abnormal phenomena should be verified by many roentgenograms and by subsequent re-examination. Serial roentgenography, at the hands of experienced roentgenologists, is efficient, but it requires expert technic and interpretation.

It is difficult for the examiner to resist a certain degree of prejudice from the fact that the patient *has been sent for examination* of the stomach and the duodenum with the implication that the referring clinician *suspects* the existence of organic disease of one or the other viscus. In law, there is a presumption of innocence until guilt is proved. In medicine, there is a presumption of disease until all suspected organs are proved to be normal, for the process of exclusion is an accepted and valuable diagnostic measure. However, among patients referred for examination of the digestive tract the greater proportion has an indefinite clinical history and the clinician doubts that they have organic disease, yet prudence requires the exclusion of a gastric or duodenal lesion. For example, at this Clinic, less than 30 per cent of the patients sent for roentgenologic investigation of the stomach or duodenum have disease of those organs, although the entire group is a selected one.

Even when gastric symptoms are pronounced, the roentgenologist should not be biased by them. Some years ago, Dr. W. J. Mayo made the significant statement that only one person in ten with gastric symptoms has a gastric lesion. If the examiner is impressed by a suggestive clinical history and searches too zealously for confirmatory roentgenologic evidence, he is almost certain to find it whether disease actually is present or not. Also, he is likely to go astray if he endeavors to base a positive diagnosis on an aggregation of petty, heterogeneous roentgenologic and clinical data. It is far safer for the roentgenologist to make his examination *without regard for the clinical facts and preferably without knowledge of them*, although subsequently he will often find it profitable to discuss doubtful cases with the clinician and to re-examine patients if necessary.

For his economic welfare, the roentgenologist is almost wholly dependent on the good will of the clinician. Moreover, the clinician's opinion seldom can be disregarded and it is often entitled to implicit respect. When, therefore, a patient is referred for roentgenologic examination with a confident clinical diagnosis of gastric or duodenal disease, the roentgenologist will, consciously or unconsciously, be inclined to confirm that diagnosis if the slightest substantiation can be found. He is likely to attach undue weight to functional alterations or meaningless eccentricities, and thus he may corroborate a diagnosis which later proves to be wrong. If he is unable to substantiate the clinical diagnosis he may, without any intent to deceive, return an extensive description of all phenomena observed, whether normal or abnormal, important or unimportant. Such reports, although they may be quite factual and non-committal, usually are susceptible of construction by the clinician as confirming his own views, which may be erroneous.

A roentgenologic diagnosis of organic disease of the stomach or duodenum is alarming to the patient. Often it carries with it the implication of necessary operation. A wrong positive diagnosis is almost unpardonable and is to be avoided if humanly possible. To avoid such errors, it will help greatly if the clinician will not expect roentgenologic confirmation of his provisional opinion as a matter of courtesy. It will help further if the roentgenologist will make no diagnosis without adequate examination, re-examine when he is *not* absolutely confident, shun verbose reports, and confine his communication to "yea" or "nay."

In sum, to avoid affirmative diagnostic errors the roentgenologist should have a thorough knowledge of normal variants and of conditions simulating disease, construe slight variations cautiously, refuse to accept indirect signs as primary bases, insist that a few roentgenograms do not constitute an adequate examination and shun all prejudice from the clinical side. There is but one safe basis for the roentgenologic diagnosis of gastric or duodenal disease; *the depiction of the lesion itself as an adventitious shadow or shadow-defect that, whether small or large, persists in form and situation, withstands manipulation and antispasmodic drugs and is demonstrable on re-examination.* Diagnoses thus founded are seldom utterly fallacious.

Finally, if anyone is inclined to assume that trustworthy roentgenologic interpretation requires neither effort nor experience, he should consider a thought from that master roentgenologist, Guido Holzknecht. On his photograph, sent to a colleague at The Mayo Clinic, he wrote in his own language a sentiment which may be translated freely as follows: "Because the roentgen picture shows something to everyone, many believe that they can find out everything from it; yet it conceals much, and it opens to me only a field for intensive study."

SECTION VI—*Abdominal Surgery*

CONSERVATIVE SURGICAL TREATMENT OF ULCER OF THE STOMACH AND DUODENUM*

By

E. STARR JUDD, M.D.†

and

GEORGE W. WALDRON, M.D.‡

ROCHESTER, MINNESOTA

MANY of the steps in our progress are directly traceable to suggestions gained from a study of the views expressed by our forebears, although in their time, their ideas may have been thought untenable. Evidently Hippocrates was none too optimistic about the future of gastric surgery for he stated that accidental wounds of the stomach were deadly. Three hundred years later, Galen commented that wounds of the stomach had been known to heal, although seldom. Early in the sixteenth century, Fallopius recommended suturing wounds. Some of the methods used to secure closure of the wounds were novel. At one time, after approximating the edges of wounds, ants' heads were employed as clips; the mandibles were aseptic by virtue of the formic acid normally present in them. After the ants closed their jaws, the bodies were cut off and the heads remained attached until the wounds were closed.

In 1810, Merren began experimental work; he attempted pylorectomy in dogs to determine the possibilities of gastric surgery. About 1876, Gussenbauer and Winiwarter resumed his work and with moderate success. Billroth likewise had been studying the problem and, in 1877, prophesied that gastric resection would be the next step in the development of surgery of the stomach. He was the first to carry out the operation successfully in man (1881) and the procedure later became known as the Billroth I operation. Pean had attempted pylorectomy in one of his cases in 1879, and Rydygier had tried it in 1880. It is probable that Nicoladoni proposed gastrojejunostomy that same year, but it remained for Wolfler to employ the operation with a good palliative result in a case of advanced carcinoma of the pylorus; he gave the operation its name. Gastrojejunostomy by the retrocolic approach was devised by Courvoisier in 1883. By 1884, Ransohoff, of Cincinnati, was performing the operation. The year 1885 found von Hacker also using posterior gastrojejunostomy and Billroth discarding his first method of gastric resection in favor of the procedure now known as the Billroth II operation.

Although a clear-cut distinction between gastric and duodenal ulcer was not made until the twentieth century, nevertheless reports in the literature indicate that gastric ulcer was recognized as early as 1600; two cases of duodenal ulcer were recorded in 1817. Even though these lesions undoubtedly are somewhat allied, they should be looked upon as distinct entities. A fact which stands out is the extreme rarity of malignancy in the duodenum and the relative frequency of malignant ulcerations in the stomach. In the few instances of primary malignancy of the duodenum which have been reported, it has been difficult to prove that the disease has been a sequel to chronic duodenal ulcer. However widely the statement may be contested, it is known that there frequently is some association between chronic gastric ulcer and certain forms of malignant disease of the stomach. Often it is impossible grossly to distinguish between carcinomatous gastric ulcer and ulcerating carcinoma.

PATHOGENESIS OF GASTRIC AND OF DUODENAL ULCER

The problem of the origin of gastric and of duodenal ulcer has been studied from the clinical, experimental, anatomic and pathologic standpoints. Approach to the study of this problem is difficult, especially experimentally, since these lesions are peculiar to man. Cohnheim divided the problem into two parts, one dealing with the cause of the original defect and one with the cause of chronicity. That an acute ulcer may become chronic is a reasonable assumption; nevertheless it is an open question whether chronicity involves fundamental principles other than those involved in the origin of the original defect. During the first decade of this century, the question of the origin of ulcers centered around the theories of Rokitansky and Virchow who believed that ulcers were the issue of the combined action of localized vascular disturbance with focal nutritional changes and the digestive action of the gastric secretion on devitalized tissue. In principle, this hypothesis is held today.

Aschoff adopted Cohnheim's attitude and attempted to explain the cause of erosions on the one hand and the factors producing chronicity on the other. He grouped the factors tending to produce chronicity under the mechanical-functional theory.

The characteristic lesions of peptic ulcer usually occur in the mucosa of the lesser curvature; they are found therefore in that region which may be exposed to an acid medium or on which the gastric contents may impinge with considerable force. Experimental investigations revealed that it was difficult or impossible to expose the gastric mucosa constantly to an acid medium by administering acid. It was believed that such exposure might be brought about by climinating the secretions that are poured into the duodenum beyond the pylorus and which tend to neutralize the acid which has not been neutralized in the stomach. When this was accomplished by various experimental anastomoses, ulcer developed in almost every instance on the duodenal side of the anastomosis. It has not been difficult to produce acute ulcers experimentally, but only recently has it been possible to produce chronic lesions.

In a series of experiments carried out in an attempt to re-

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†Head of Section in Surgery, The Mayo Clinic.
‡Fellow in Surgery, The Mayo Foundation.
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produce the changes in the liver resulting from the use of cinchophen, Bollman found that gastric ulcer developed in some dogs after use of the drug. According to our experience, there are few instances in which gastric ulcer develops after taking ordinary chemicals into the stomach.

Infection and inflammation undoubtedly play a part in the etiology of ulcer of the stomach and of the duodenum. A striking example of this is the rather extensive gastritis that is found in some cases. It is surprising how well some of the patients get along after foci of infection are cleared up. This is an important consideration in the conservative treatment of ulcer of the stomach and the duodenum. However, in many of the cases, it will be found that infection is not responsible for the original development of ulcer.

Knowledge of the pathogenesis of ulcer has remained almost stationary in spite of the great amount of research work done. One thing which we have learned about this phase of the subject is that certain types of individuals are more likely than are others to have peptic ulcer. This is particularly true of duodenal ulcer. Often the condition responsible for the digestive disturbance is not true duodenal ulcer but rather, an inflammatory process which has been designated "duodenitis." There may be no demonstrable break in the mucosa, although occasionally pin-point ulcerations may be found. The roentgenologic examination will disclose a deformity of the cap of the duodenum without any sign of a crater. A history of hemorrhage is common in this group of cases.

Many of the patients in whom these lesions develop are of nervous temperament; they are likely to be artistic and highly intelligent. Unfortunately, this type of person does not respond well to surgical treatment. The result of almost any operation is likely to be unsatisfactory, partly because of the functional nature of the complaint and partly because of the tendency to form secondary lesions. In cases with such a background, surgical treatment should be avoided until it is evident that it is absolutely necessary because of persistent pain, hemorrhage or obstruction.

We know that the chemical action of pepsin-hydrochloric acid, trauma to the mucosa, infection or toxins, a poor general systemic condition and irregular habits of living are factors in the development of peptic ulcer. Any logical treatment of peptic ulcer, whether medical or surgical, must be directed toward correction of these recognized etiologic factors.

GASTRIC ULCER

We know that sometimes the symptoms of gastric ulcer may be relieved more readily through a medical regimen than are those symptoms resulting from duodenal ulcer. In a few instances in which there is reason to feel that the lesion is benign, one might be justified in offering a trial of medical management providing the patient can be kept under close observation. Up to the present time, we have no clinical or roentgenologic criteria which will determine whether there is an area of malignancy in the border of a chronic gastric ulcer, and so it is evident that the lesions must be removed and microscopic study made before we can be certain of the nature of the lesion. In certain patients, the symptoms will subside and the large crater defect produced by a gastric ulcer will not be visible after a short period of rest, relaxation, and dietary regimen. Nevertheless, if exploration is made at a time when it is presumed that ulceration is almost healed, one may find that he has been deceived, and that there is still a fairly prominent ulcer present. Probably we have all had this experience and so there can be no question but that such a situation obtains in at least some of the cases in which patients are comparatively symptom-free under carefully regulated regimens.

Even in the light of present day methods of diagnosis and greatly improved medical treatment, we think that early operation is advisable. However, it should be emphasized that when this is carried out, it should be as conservative as is consistent with the extent and the nature of the lesion. For a number of years, it has been the practice in this clinic to recommend surgical treatment to practically all patients with gastric ulcer. From the varied and meager attempts toward operative treatment made in the nineteenth century, the surgeons of the twentieth century have developed some of the present methods of treatment. Many of the operations originally were planned to remove a malignant process or to relieve symptoms caused by neoplastic growths. Some of these similarly are employed today; others have undergone modification in accordance with our increased knowledge of peptic ulcer.

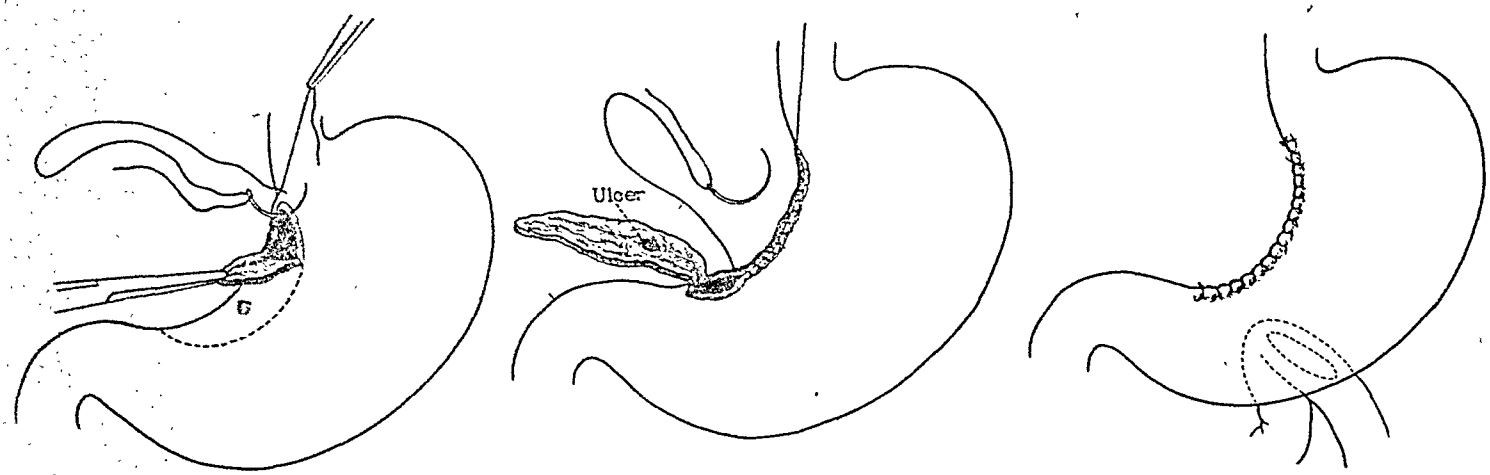


Figure 1—Excision of gastric ulcer and posterior gastrojejunostomy. A wide excision is made which includes most of the lesser curvature of the stomach.

Formerly, in a large proportion of patients, treatment consisted of gastrojejunostomy alone. It was the operation of choice for both gastric and duodenal ulcers. It proved a suitable procedure in many instances because the disease had been allowed to progress to an advanced stage but, with developments in surgical technic and the opportunity to diagnose the condition earlier, excision of the lesser curvature and gastrojejunostomy justly gained in popularity (Figures 1 to 3). Approximately 90 per cent of gastric ulcers are situated along the lesser curvature. Eighty per cent of the lesions are small, and many of these probably are best treated by this method. The operation has been so satisfactory in our experience that we perform it frequently. Often, on account of the size of the ulcer, resection of the stomach would be easier from a technical standpoint but, if the ulcer is of moderate size, excision and gastrojejunostomy will give a very satisfactory functional result. For some unknown reason, jejunal ulceration seldom develops after this procedure. It is significant that, during a period of twenty-six years, only thirteen patients were subjected to operation for

jejunal ulcer occurring subsequent to this operation, and two of these had had both gastric and duodenal ulcers. About 6 per cent of all patients with gastric ulcer will have multiple lesions; in these, partial resection of the stomach is required.

In reviewing the operations for gastric ulcer performed by various members of the staff of The Mayo Clinic during

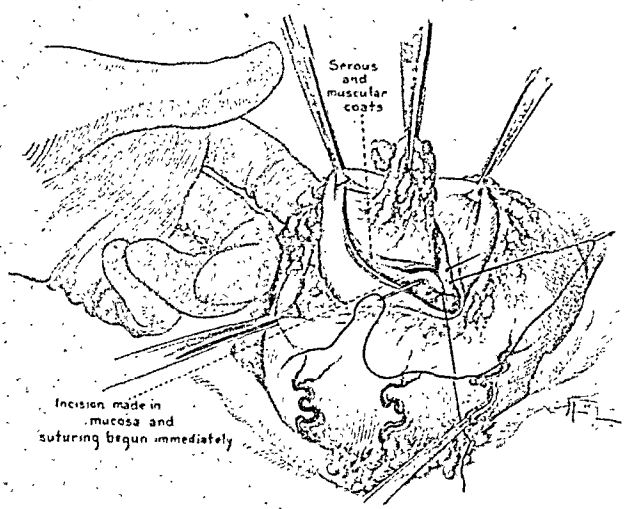


Figure 2—Detail of early step in excision of gastric ulcer.

a period of twenty-six years (1906 to 1931 inclusive) we find that a diagnosis of malignant ulcer was made in 791 cases and of benign ulcer in 2,276 cases. Another interesting observation is that the *immediate* operative mortality rate

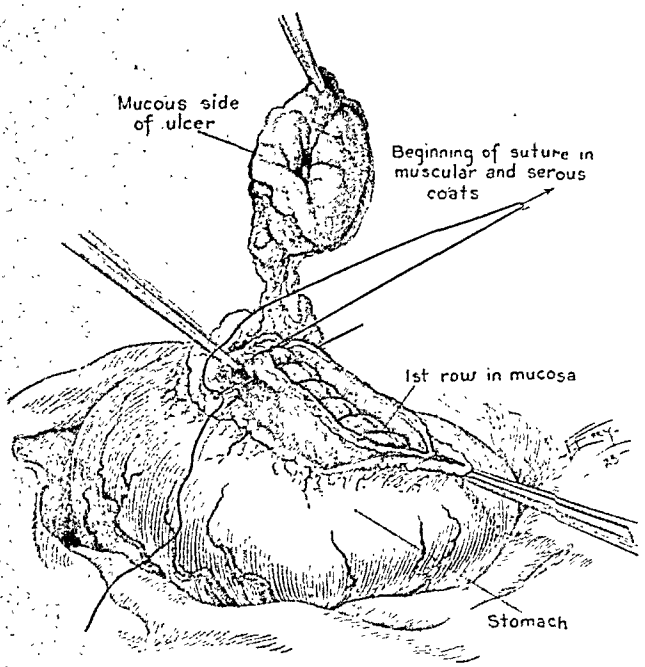


Figure 3—Detail of closure after excision of gastric ulcer.

among patients with *simple benign gastric ulcer* was about half of that occurring among patients with *malignant change* in the lesion. These twenty-six years span practically the most active period in the development of gastric surgery; the operations performed were of a varied nature: In 211 cases, the lesion was excised and nothing further was done, although in twenty-nine cases malignant change in the ulcer was recognized at the time of operation. Removal of the ulcer and gastrojejunostomy was the procedure employed in 857 cases of benign ulcer and in forty-three cases of malignant ulcer.

DUODENAL ULCER

Again and again, healed duodenal ulcer has been observed. Realization that such lesions do heal of their own accord is responsible for the feeling that if the lesion is of short duration and is not extensive, adjustment of the patient's activities may obviate the necessity for operation. In some circumstances, therefore, it will be permissible, and in others advisable, to give the patients with duodenal lesions an opportunity to try medical treatment. The measure of success to be derived from the plan in selected cases will depend upon strict adherence to a carefully regulated regimen. Some high-strung individuals will have recurrence even though the lesion has been removed or has been made to heal. For this reason, any operation may give unsatisfactory results, and particularly gastrojejunostomy. Although we know that many patients with duodenal ulcers and duodenitis do obtain relief through adoption of a carefully regulated medical and dietary regimen, also we are convinced that there are others whose only hope of recovery from the distressing syndrome lies in surgical intervention. Perforation of the lesion, obstruction, hemorrhage or recurrent symptoms, in spite of well-controlled management, constitute the chief indications for surgical intervention. However, when this is carried out it should be a conservative plan of procedure.

It is interesting to follow the development of the surgical procedures for duodenal ulcer at this Clinic and elsewhere. In 1881, digital dilatation of the pyloric sphincter was proposed by Loretta, thus indicating that the influence of sphincteric action has been recognized for at least fifty years. A plastic operation on the pylorus was carried out independently by Heineke, in 1886, and by Mikulicz, in 1887. At this time Rydygier suggested resection of bleeding ulcers and with this pyloroplasty. About 1889, Mikulicz attempted suture of a perforated ulcer. His patient died, but Kriege successfully employed the operation in one of his cases three years later. Our records show that the date of the first local operation for duodenal ulcer to be performed by a member of our Staff was about 1896 and that it was carried out according to the Heineke-Mikulicz technic. By 1902, we were excising duodenal ulcers. Gastrojejunostomy also was being employed. At that time, however, the number of patients undergoing surgical treatment was limited and a just appraisal of the results of operation was difficult to obtain.

Each year more excisions of duodenal ulcer were carried out. It became more evident that the tonicity of the pyloric sphincter-muscle had a great deal to do with the success or the failure of the procedure to relieve symptoms. It was thought that division of the pyloric sphincter-muscle, in addition to excision of the lesion and closing the defect transversely, might offer solution of the difficulty. The percentage of cases in which good results were obtained seemed to increase following this procedure, but a study made sometime afterward revealed that the sphincter soon regained much of its former activity and then quite frequently interfered with proper emptying of the stomach.

Both in this country and abroad, several types of pyloroplasty were being employed with varying degrees of success. Since some of these procedures were followed by recurrent ulceration, it was evident that the problem had not been solved. Finally, a more extensive operation was planned to insure elimination of sphincteric action: the cap of the duodenum was excised together with the anterior part of the pyloric sphincter-muscle and closure was made as a gastroduodenostomy. This procedure, first employed in 1924, maintained normal physiologic action and materially reduced the number of recurrent ulcers. It was found that, even after several months, the pyloric outlet would exert some measure of its former function, and so, in succeeding cases, a greater part of the pyloric sphincter-muscle and lower part of the stomach were excised until it was found that removal of from two-thirds to three-fourths of the sphincter-muscle produced the desired effect (Figures 4 to 7). A sufficient

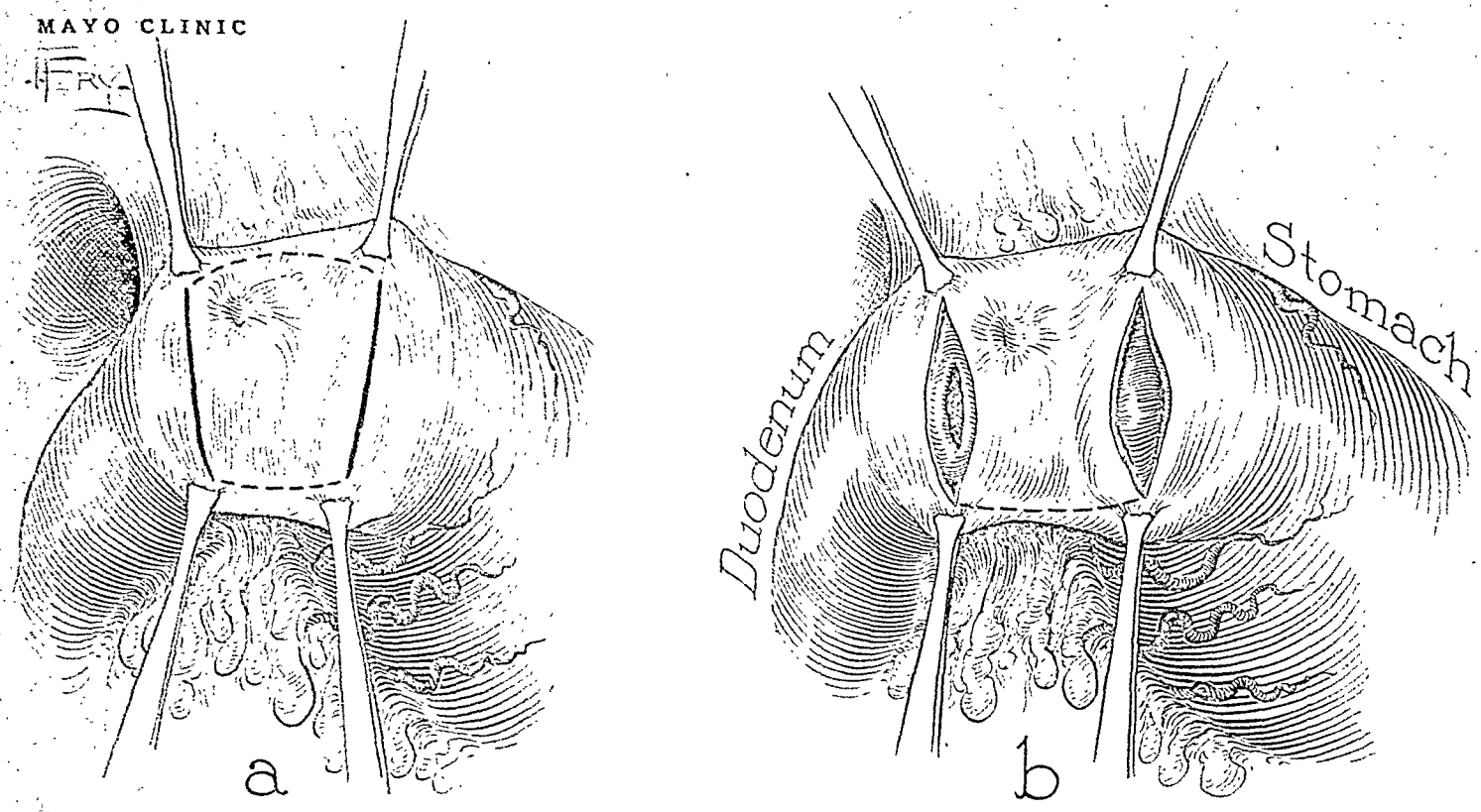


Figure 4—(a) Plan of incision, prior to excision of the duodenal cap; (b) Parallel incisions in the duodenum and stomach.

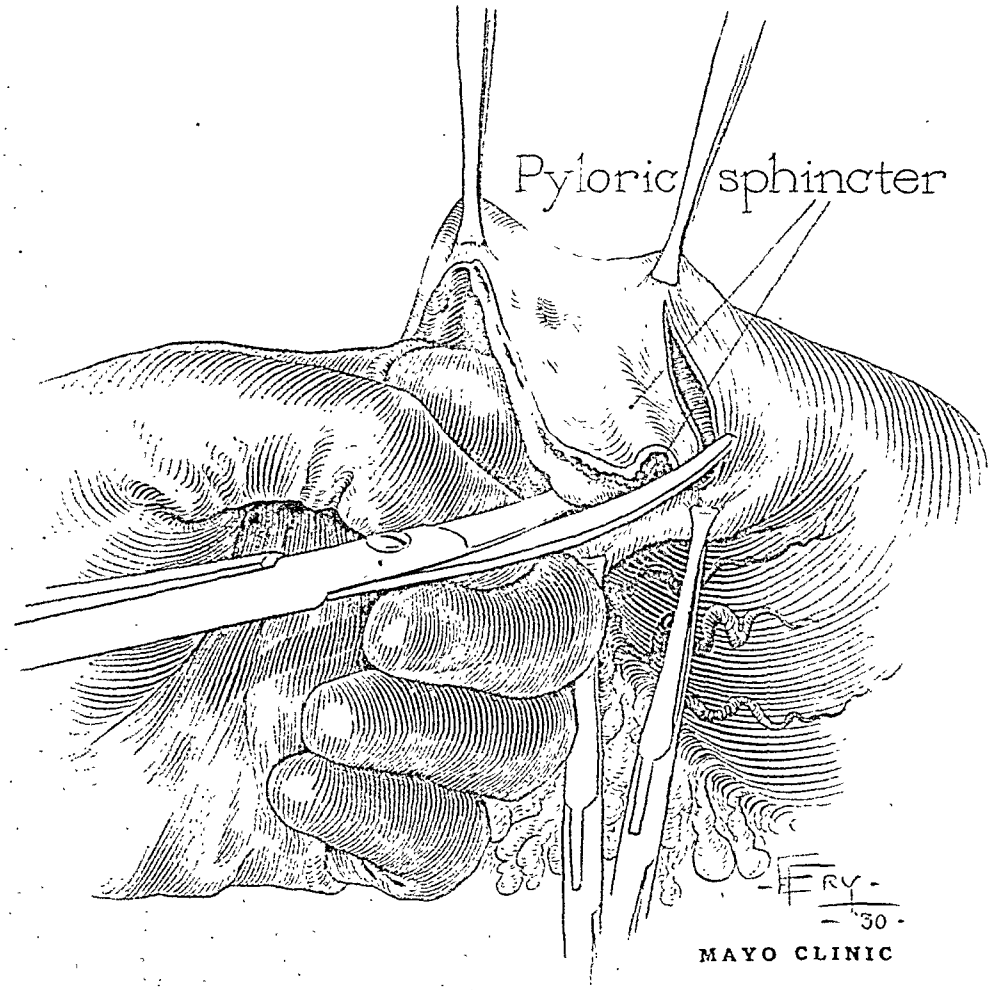


Figure 5—Cutting across the pyloric sphincter muscle, following the procedure illustrated in Figure 4.

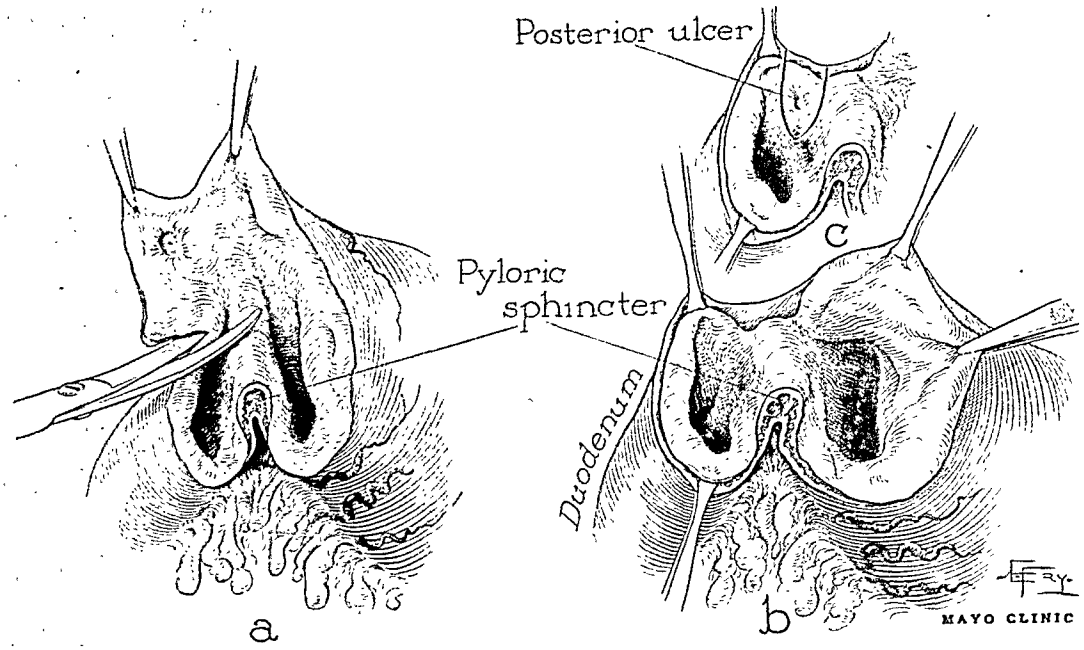


Figure 6—Procedures employed after those illustrated in Figures 4 and 5 have been completed. (a) Completing the excision of the cap of the duodenum, anterior part of pyloric muscle and a portion of the stomach, without the use of clamps; (b) Excision completed; (c) Extending the incision to remove an ulcer on the posterior duodenal wall.

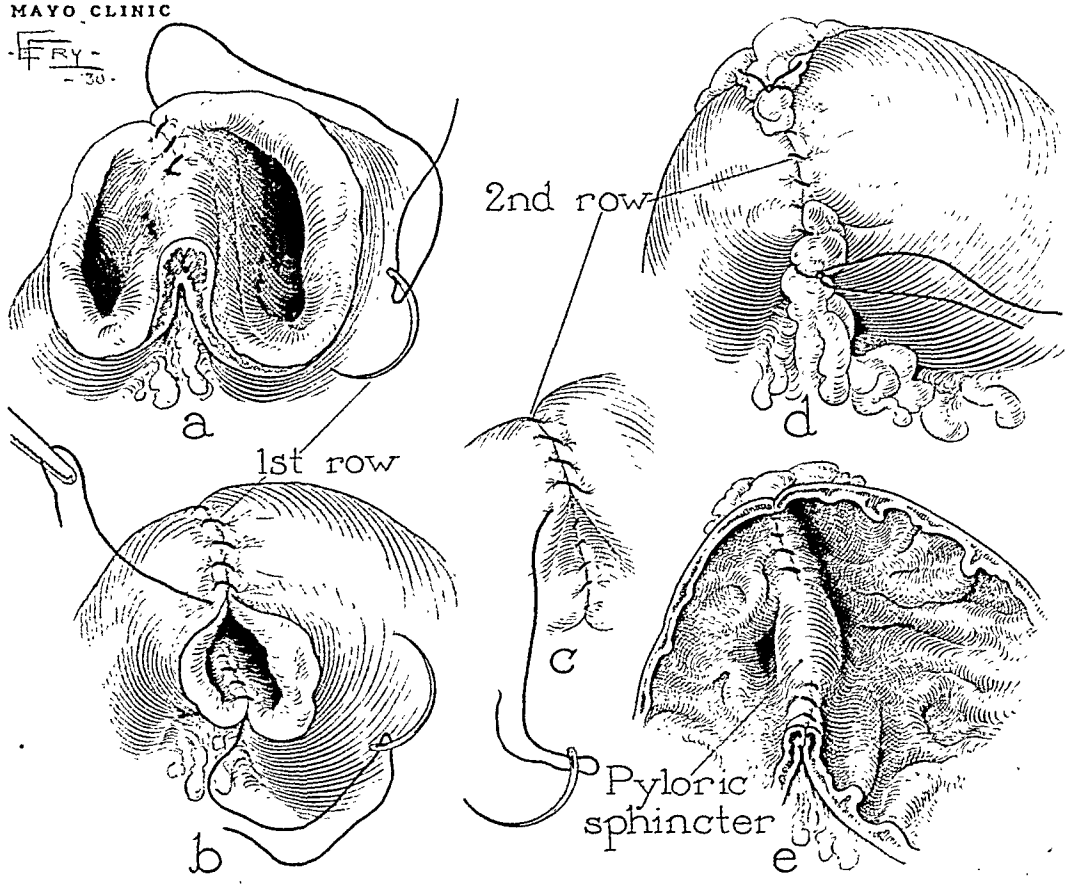


Figure 7—The last steps of the series illustrated in Figures 4, 5 and 6. (a), (b), (c), (d), Steps in making the closure in gastroduodenostomy; (e) Cross section of the completed closure in gastroduodenostomy.

portion of the muscle must be excised to overcome the spasm which is known to be an important factor in the production of symptoms. At first, it was felt that, in order to justify the operation, it must be possible to mobilize the duodenum readily, but experience has taught that adequate exposure of the operative field will increase the ease of performing the technical steps without undue risk. The operative mortality-rate with the procedure now is almost *nil*. In this clinic the operation has been performed in more than 900 cases and but adhesions had interfered with normal emptying of the stomach.

The procedure described is particularly applicable to cases in which the lesion is in the form of duodenitis. In a few instances it has been employed for marked hypertrophy of the pyloric sphincter-muscle and has given satisfactory relief. An ulcer on the posterior duodenal wall usually will heal after this operation. Especially is this true if the lesion is in the nature of duodenitis. Should there be a large crater

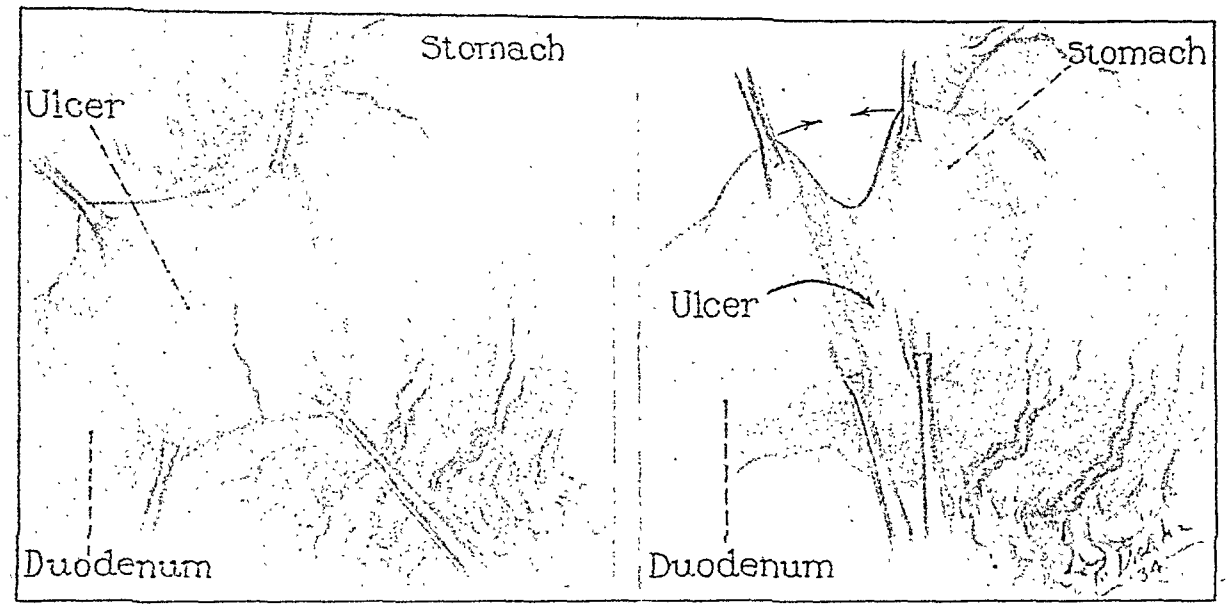


Figure 8—*Left*, Selection of the site of the anastomosis between the pyloric end of the stomach and the first portion of the duodenum in gastroduodenostomy. *Right*, Approximating duodenum and stomach.

the ultimate results have been satisfactory. In some patients, symptoms do recur, but if the patient is operated upon a second time, an ulcer seldom is found. In most of these instances, failure to obtain relief apparently has been due to adhesion of the operative field to the parietal peritoneum or to the adjacent viscera; the duodenal lumen was adequate on the posterior wall, it will be found best to extend the incision and to excise the lesion. However, it is not expected that a single procedure will be suitable for all cases. Very likely there will always be a small percentage of patients who will fail to respond to treatment regardless of the kind of attention given, but the number of complications which arise

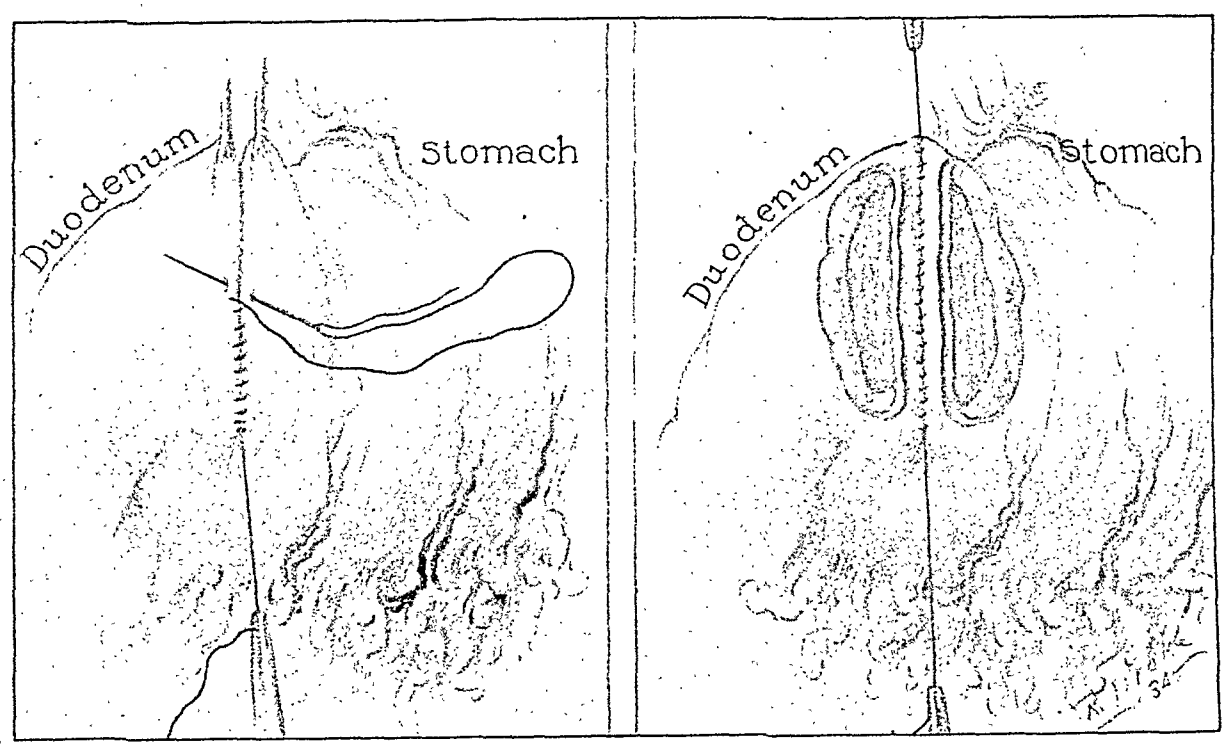


Figure 9—After the approximation illustrated in Figure 8. *Left*, Posterior row of sutures. *Right*, Opening the stomach and duodenum.

following this operation will be minimal compared with the incidence of jejunal ulcer after gastrojejunostomy.

In order to avoid the disasters of gastrojejunostomy and to retain the advantages of more normal gastric physiologic action in cases in which excision of the cap with the lesion and part of the pyloric sphincter is not feasible, lateral gastroduodenostomy has been employed. To Jaboulay is attributed the first suggestion (in 1892) of the possibilities of this procedure. During this same period, Halsted was working on a modification of pyloroplasty, using lateral anastomosis. In 1898, Henle made clinical application of lateral gastroduodenostomy; he gave Mikulicz credit for the plan. Finney stated that his gastropyloroduodenostomy, better known as Finney's pyloroplasty, was the outgrowth of that work.

In the gastroduodenostomy which has been employed by us, the pyloric end of the stomach is anastomosed to the first portion of the duodenum, without disturbing the pylorus and without excision of the duodenal ulcer (Figures 8 to 11). The porcedure is completed as one would perform gastrojejunostomy without clamps. This operation technically is applicable to almost any case of duodenal ulcer, for there is no need for mobilization of the duodenum. Wilkie has employed a somewhat similar procedure, except that he makes an anastomosis to the second portion of the duodenum and, frequently, considerable dissection is required. He has reported satisfactory results in about 89 per cent of patients who have been observed from one to twelve years afterward. In only two of these has stomal ulcer been demonstrated and, in these, gastroduodenostomy apparently had not had any

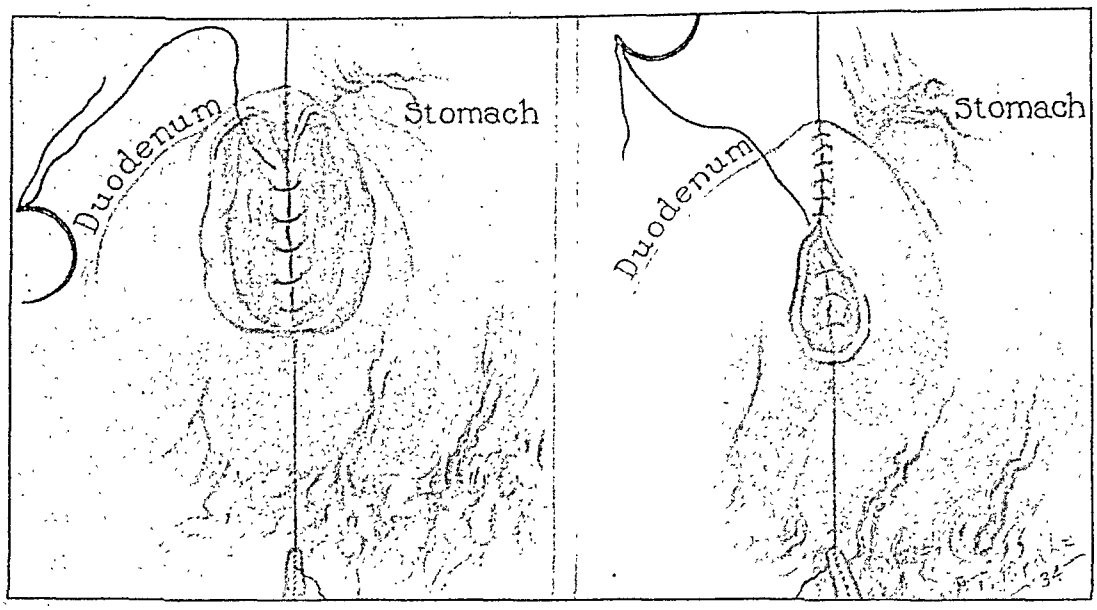


Figure 10—Steps succeeding those illustrated in Figures 8 and 9. The anastomosis is carried out in the same manner as in gastrojejunostomy.

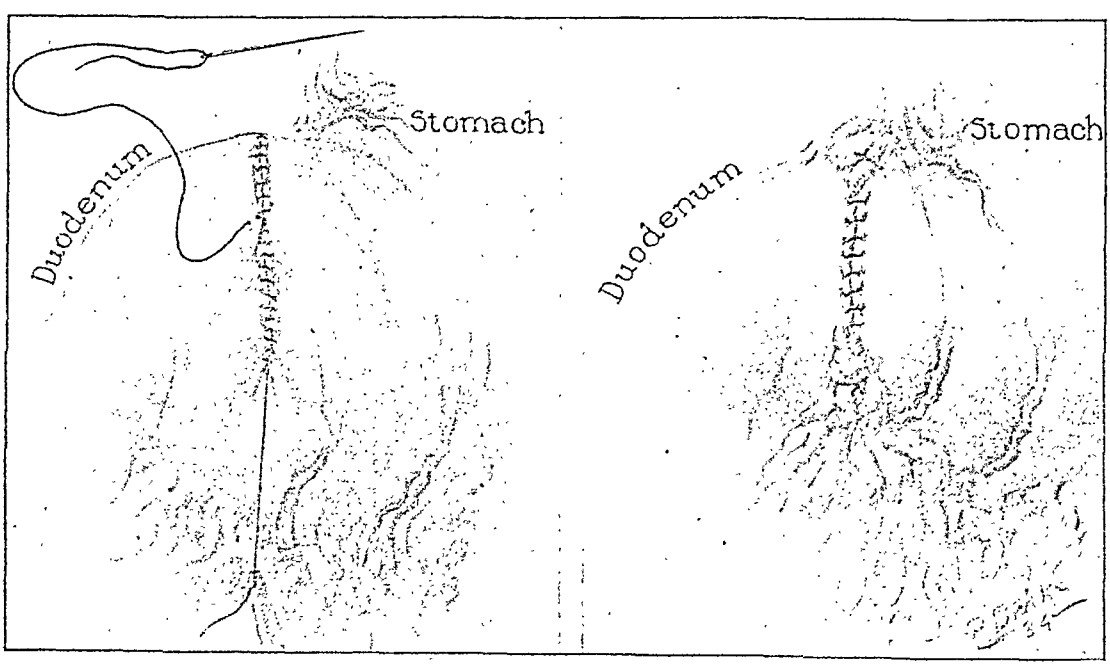


Figure 11—Last steps in the series illustrated in Figures 8, 9 and 10. Completing the closure.

effect upon the original duodenal lesion although, in each instance, marked lowering of gastric acidity had occurred. We have not encountered a recurrent duodenal ulcer or a stomal ulcer in cases observed for the past one to ten years in which lateral gastroduodenostomy had been performed. Report of an unsatisfactory result has been obtained in only one case. This patient found it necessary to continue the use of a modified ulcer regimen and alkalies.

From time to time, partial gastric resection has been advocated and carried out for duodenal ulcer on the theory that such operation removed the acid-producing portions of the stomach. More recent studies have indicated that most of the acid-producing cells are situated in the fundic and cardiac parts of the stomach, which of course nullifies the argument for this radical procedure. It is now realized that, in this country, most surgeons do not encounter many lesions of the type similar to that with which European surgeons must contend, namely, the peptic ulcer with extensive associated gastritis. For these reasons, here we do not feel justified in adopting this radical operation. Also, it is probable that resection of the greater portion of the stomach does not offer any better protection against stomal ulcer than does simple gastrojejunostomy; furthermore, radical operation makes any future surgical treatment for ulcer difficult and hazardous.

The trend of surgery, at this Clinic, for acute and chronic duodenal ulcer and duodenitis is apparent. Of 2,303 patients receiving attention for these conditions in the past five years, 1,472 underwent only gastrojejunostomy and 663, local operations. Less than 5 per cent were subjected to the radical procedure of partial gastrectomy. This indicates the attempt which is being made to maintain normal physiologic conditions and to avoid extensive resection which many times turns out to be unsatisfactory in the end.

In selected cases, gastrojejunostomy continues to be a useful operation for the treatment of duodenal ulcer. It is particularly satisfactory for older patients and especially those in whom symptoms of obstruction have developed. It was employed in the early history of this Clinic and then seemed to be a highly satisfactory procedure, for not a patient was operated upon for jejunal ulcer until 1912. With more accurate knowledge of the type of case for which the operation is suited, in recent times, subsequent complications have been materially reduced.

JEJUNAL ULCER

It is impossible to make an accurate estimate of the incidence of jejunal ulcer. The lesion is more frequent among men than among women, and apparently is more common among Teutonic and Semitic peoples than among Anglo-Saxons. We know that it occurs a great deal more frequently after gastrojejunostomy for duodenal ulcer than it does after the procedure for gastric ulcer. Various investigators have estimated its incidence at from 2 to 40 per cent. In a period of twenty years (1912 to 1931), 628 patients were operated on for jejunal ulcer by members of our staff. Jejunal ulcer was a sequel to gastro-enterostomy for *duodenal ulcer* among 609 of these patients. Of the nineteen cases in which it followed that procedure for *gastric ulcer*, in seven patients, duodenal ulcer also was present. These figures also seem to substantiate the contention that there must be considerable variation between the etiologic factors in gastric and duodenal ulcer. They indicate the relative safety with which the jejunum can be joined to the stomach in operations for benign ulcer proximal to the pylorus. Wilkie stated that, in his experience, the most effective preventive measure was to avoid gastrojejunal anastomosis in all cases of duodenal ulcer in which there was high acidity and little or no stenosis and to employ either gastroduodenostomy or some other form of plastic operation at the pylorus in such cases. Also he recommended eradication of septic foci in teeth, tonsils, appendix, and gallbladder as an essential part of the treatment of peptic ulcer.

CONCLUSIONS

When once a jejunal ulcer has formed, the most logical treatment is to disconnect the gastrojejunal anastomosis (removing the ulcer), close the openings, and restore the gastro-intestinal tract to its normal continuity. If the original lesion still is active, or if it has caused sufficient scarring to interfere with the patency of the pylorus, one of the two local operations for duodenal ulcer should be utilized.

As has been stated, a medical regimen has a definite place in the treatment of peptic ulcer. In certain circumstances, it is the only plan which is justified. The degree of satisfaction to be derived from the regimen usually depends upon the patient's temperament and his ability to adhere strictly to the plan.

It does seem that there should be some rather simple plan of management which would obtain control of duodenal ulcer, especially among young people who have had symptoms only a short time and who have not experienced any severe attacks. Undoubtedly, if these individuals in the early stage of the disease could receive treatment, the number requiring subsequent surgical intervention would be reduced.

The possibility of malignant change in gastric ulcer must be kept foremost in the mind of anyone employing a medical regimen for this condition. A medical regimen should be continued only on its demonstrated merits in the particular case. In a few instances, it may be given a trial if there is reason to believe that the lesion is benign and the patient can be kept under close observation.

When surgical treatment is instituted, either for gastric or duodenal ulcer, it should be conservative. The results of excision and gastrojejunostomy amply justify this procedure for gastric ulcer.

Several methods of treatment of duodenal ulcer now are available which are satisfactory when properly applied to the conditions for which they are appropriate. Gastrojejunostomy is a useful procedure in selected cases. Removal of the duodenal lesion is desirable whenever this can be accomplished without undue risk. Relief of spasm at the pylorus affords additional advantage. There has been much justification for the increasing use of the operation by which the duodenal lesion and part of the pyloric musculature are excised. Gastroduodenostomy without removal of the lesion has been used sufficiently often to demonstrate that it offers a very good prospect of relief in the cases in which it is indicated.

Further developments in the treatment of ulcer of the stomach and the duodenum will be delayed until more is learned about the etiology and pathogenesis of these lesions. At present, among the *clientele* of most surgeons in this country, there seems no good reason for radical resection for duodenal ulcer.

AN ANALYSIS OF THE RESULTS OF BILIARY TRACT SURGERY*

By

JOHN TILDEN HOWARD, M.D.

BALTIMORE, MARYLAND

AS ONE scans the many papers which have appeared in the last ten years concerning the results of surgery of the biliary tract, he cannot avoid the observation that the reporters and analysts of these results have been in the main, surgeons. Now, being of Dr. Cushing's genus *Homo chirurgicus* does not mean that one cannot be a perfect and an impartial essayist of the results of surgical treatment. However, it is quite natural for the surgeons to be charitable toward surgery; just as natural as for the general practitioner and the internist to be somewhat critical of surgery, since to them come the disappointments of such therapy.

Goldish and Gillespie[1] have summarized the results of biliary tract surgery as reported in the literature over an eight-year period. Though it must have been most difficult for them to reduce to a common denominator the varying criteria of cure, they have stated that, in a total of 5,637 cases which had been followed by different observers, 74% were considered well, 16.1% had been improved and 9.9% reported no relief from biliary tract surgery. Judd and Priestley,[2] after a careful study of a large number of patients followed many years after their operations, reported, "Good results were obtained following cholecystostomy in 60% of cases and following cholecystectomy in about 84%."

It has been interesting to us to compare these figures with a follow-up study of a relatively small group of private patients of Dr. Thomas R. Brown. The group consisted of 84 patients who had complete and medically detailed office records, who had been studied at length by Dr. Brown and who had had surgical exploration of the biliary tract at his advice from two to fifteen years before this study was made. No patients were included who had been seen in only a single consultation or very briefly on other services in hospitals. Needless to say, in all of the 84 patients, gallstones or inflammation of the biliary tract was diagnosed before operation; no cases of suspected malignancy, of hepatic cirrhosis nor cases of abdominal exploration without a fairly definite diagnosis of gall tract disease were included. Operative notes were available on all of these patients. Of the 84 cases who had had preoperative diagnoses of biliary tract disease, such disease was found by the surgeon (and in most cases by the pathologist) in all but six.

Findings at operation. Of the 59 cases diagnosed as *acute or chronic cholecystitis with gall stones*, this diagnosis was completely confirmed in 57. The fifty-eighth case showed gallbladder inflammation with bile "mud," and the fifty-ninth revealed a gallbladder which, to the surgeon, seemed to be normal. Under "medical pressure", he removed the gall sac and the pathologist reported "chronic gallbladder." *Cholecystitis* alone was diagnosed 25 times and it was found alone in 14 of these cases; it was associated with gallstones in eight others. The cholecystitis diagnosed was not found in three cases. Adhesions or a mildly inflamed appendix seemed to be the only organic basis for symptoms in two; a third had a normal gallbladder.

Operations performed. Cholecystectomy was performed 63 times as a primary operation and four times after previous cholecystostomy. In this series, *cholecystostomy* was done on 13 patients. Once a *cholecystogastrostomy* was the operation of choice and once a *choledocholithotomy* was done for a stone which, presumably, had been overlooked at a previous cholecystectomy. In two cases, no surgery was done other than the separation of adhesions in the right upper quadrant and removal of the appendix.

Mortality. Four of the 84 patients died in the hospital of operative or postoperative complications. This was a surgical mortality of 4.7 per cent. The *exitus* of one was *via* postoperative pneumonia; of another, operative shock; a third developed intestinal obstruction and died after a second operation; the fourth developed a bile sinus which eventually communicated with the peritoneal cavity and produced a general peritonitis.

Methods of collecting postoperative data. Admitting its defects, we have believed the questionnaire method of determining the present conditions of the surviving patients to be the most practical. Also we have had the opportunity of personally questioning and of re-examining a number of the patients in this group. Our questionnaire was similar to that of Cattell[3] of Lahey's Clinic. We asked for replies to the following questions: 1. Have you had complete relief from your gallbladder symptoms? If you have not obtained complete relief, what symptoms have you had? 2. Have you been jaundiced since the gallbladder operation? 3. Do you complain of gas, belching, a feeling of distension or of indigestion? 4. Have you had further operations or X-ray examinations? 5. Have you other abdominal complaints?

Eighty questionnaires were mailed. Seven were returned by the postal service because the persons could not be found. Eight patients were not heard from; two had died between the dates of their discharges from the hospitals and that of the questionnaire. Sixty-three returned to us more or less detailed reports about themselves and their symptoms. From these replies and with the aid of our general knowledge of the patients (every history had a more or less comprehensive note about the patient's nervous state) the cases were classified after the manner of Davis.[4] The first group contained those patients who seemed to have been completely cured, i.e., there were left no symptoms to remind the patient of his old trouble. In the second group were the relatively cured or those who had obtained relief from all the more disagreeable symptoms but who occasionally had mild upper abdominal discomfort. The third group was termed "improved" and it included those patients who still had symptoms but who were better than they had been before operation. In the fourth group were those who had not been helped by surgical procedures.

Status of patients postoperatively. From the replies to our questionnaires and from our knowledge of the patients, we concluded that 28 (44.4 per cent) of the 63 who had answered us had been completely cured by surgery. Ten (15.8 per cent) had been relatively cured; 12 (19.0 per cent) were "improved;" 13 (20.6 per cent) were not improved.

Answers were received from 49 patients who had had cholecystectomy as their primary biliary tract operation. Twenty-five (51.0 per cent) of them were unquestionably cured. Six (12.0 per cent) were relatively cured. Nine (18.0 per cent) were "improved" and nine were not improved. Nine of the 13 patients who had had cholecystostomy replied to our questions. Two of them seemed to be really cured. Three were relatively cured; two were "improved" and two were unimproved. Three of the four persons who had had cholecystectomy after an earlier cholecystostomy replied. The second operation had completely cured one; one was relatively cured and one was unimproved. The patient who had had a cholecystogastrostomy for a pancreatitis associated with a cholecystitis was "improved." One patient who had had upper right quadrant adhesions was unimproved by appendicectomy and the separation of these adhesions.

*From Gastro-Intestinal Clinic, Johns Hopkins Hospitals.
Submitted for publication, April 24, 1934.

From the data in this small series of cases, again it is apparent that cholecystectomy is the operation of choice when surgery is indicated for the treatment of cholecystitis with or without stone. With it, two patients out of three have received striking and satisfactory improvement (they have been cured or relatively cured.)

Judgment of the success of a biliary tract operation is not based alone upon the removal of pathologic tissue. It should also be based upon the degree of relief from the clinical symptoms which led to operation, on the symptoms which it failed to relieve and on any late ill effects. How frequently we review the hospital record of "Mrs. Smith" who has consulted us for a dyspepsia which she had before a biliary tract operation and which has remained after the operation! In the handwriting of the Resident Surgeon, we see on the first page of the record, "*Diagnosis:* Cholecystitis, chronic; cholelithiasis. *Operation:* Cholecystectomy. *Result:* Well." If the diagnosis was correct, Mrs. Smith was well, surgically speaking. Certainly she was cured of her chronic cholecystitis. But *here she is*, complaining of symptoms referable to the biliary tract, as she did before her operation, and, medically speaking, we cannot say that she is well or that her operation was a real success. It would be unfair for us to say that her operation was not indicated, but we must find trouble elsewhere than in the liver and its ducts before we group her with the successes of biliary tract surgery.

Of course, the published reports of surgeons actually are not based upon the discharge notes of hospital histories. However, the surgeons are notorious optimists and, as such, they may be prejudiced judges. A critical study of the results of biliary tract surgery seems to be within the province of the internist and more data from his point of view should be made available.

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ABSTRACTS

WORKMEN, E. WALTER AND MILLER, G. GAVIN.

A Clinical Review of Two Hundred and Forty-One Cases of Obstruction of the Small Bowel. Can. Med. Ass'n Journal. Vol. 30, February, 1934, Vol. 30, No. 2.

The death rate in intestinal obstruction ranges from 40 to 50%. According to Vick the mortality averages 38.8%. Notwithstanding the saline therapy and the study of the X-ray films, the mortality remains high. The authors have tried to investigate into the 241 cases who were admitted to the Royal Victoria Hospital, during the last eleven years. In their study they have voluntarily excluded the obstructions following appendectomy, the paralytic ileus and the large bowel obstructions. After an extensive discussion on the delays as an etiological factor of mortality—"90% could be saved if they reached the operating table in six hours,"—the errors of the purgatives and the betrayal of morphine, the principal signs are pointed out: 1. the rhythmical crampy pain; 2. the vomiting and; 3. later the distention of the abdominal wall. Physicians must bear in mind that a first enema might be effectual because the bowel below the site of obstruction contains feces. Then follows an explanation of the sequence of the vomiting; colicky pain, visible peristalsis borborygmi, distention, dehydration and toxaemia. It seems experimentally that distention of the bowel causes death earlier than dehydration.

Gangrene is to be feared.

Of the 241 cases of complete small-bowel obstruction, 156 were classified as strangulated external hernia, 85 were due to internal causes. The mortality in cases of hernia was 87% while in the second class the mortality rose to 51.7%; for all cases it was 27.82%; 77% of hernia cases were operated upon within the first 48 hours, while only 45% of cases due to internal causes were led at this stage to the operative table. The authors can not support the tendency of surgeons delaying the operation until a definite diagnosis is assured. Operating with the signs of "an acute abdomen" present is less hazardous than is delaying. One should not rely too much upon the inconsistent images of the X-rays.

Films are not valuable when the patient is X-rayed lying on the side or in the up-right position: distention of the bowel by gas and the presence of fluid levels are amongst the more important findings in such cases. The presence of gas only, contrary to Ochsner's belief, might lead to gross errors.

The *white blood* count averages between 11,388 and 12,886, with some greater numbers, in cases of simple obstruction or strangulated obstruction, without any inflammatory condition. The majority of the patients showed a *temperature* normal or subnormal. The pulse rises rapidly in most cases "and is a useful guide to prognosis." It seldom exceeds 100°F.

The *loss of fluids and sodium chloride* in the gastro-intestinal secretions, as well as the loss of free hydrochloric acid in the stomach secretion allows a true explanation of the increase of the nitrogens (non-protein) and of the success derived from the intravenous injections of hypertonic sodium-chloride solutions. In cases of strangulated obstructions, patients cannot be prolonged with such injections as in those of simple obstruction.

"The loss of chloride and dehydration play a minor role as a causative factor of death where strangulation is present."

The authors' operative mortality appears falsely high, as most of the cases where a simple enterostomy or entero-enterastamosis was performed, proved of a most serious nature.

Resection is to be avoided in gangrene where there is the least doubt, as to the color of the loops.

Enterostomy (Vidgoff) should be performed with great caution.

Jean R. A. LeSage.

BERGERET, A.

Apropos de la gastrectomie avec implantation gastro-jejunale. (Gastrectomy with gastrojejunal implantation). Rev. de Chir. 53: 82-108. January, 1934.

In a total of 775 interventions for gastroduodenal affections, the author has performed 372 gastrectomies, in most cases with gastro-jejunal implantation. His technic, after a series of simplifications, is described and well illustrated, step by step.

In an earlier series of 243 gastrectomies there were 20 deaths (8%) due largely to pulmonary complications, as compared with a mortality of 3%. The study of late results in the patients operated upon in 1926 and 1927 (reported in Presse Med. Dec. 5, 1931, p. 1796) showed perfect function in more than 70% of the cases. Changes in technic, based on this review of cases, enabled the author to obtain perfect results quite regularly. Pain and vomiting disappeared completely, digestion was good, strength was regained and at the end of two or three months the patients returned to normal life.

The total immediate mortality in subtotal gastrectomy for cancer has been 15% (119 gastrectomies, 18 deaths). Taking only the recent series, the mortality is 3% or the same as in ulcer cases. Some of the patients have lived over five years, one for eight years. Exact figures are not available, but the author believes the average life is 18 months; and death is almost always due to recurrence in the liver and in the glands.

H. L. B.

ROBERTS, CARL G.

Transduodenal Decompression and Reintroduction by Proctoclysis of Gastrointestinal Drainage in Acute Mechanical Ileus. Jour. Am. Med. Assn., 102:1149 (April 7) 1934.

The author reports the case of a woman of 45 years of age who was operated upon for a perforated gangrenous appendix. Many complications followed and among these a bulging of the *cul de sac* and a marked elevation of the right diaphragm with their accompanying symptoms led to two operations, one, a posterior colpotomy through which 500 c.c. of pus was evacuated and the other, a ninth rib resection with entry into the sulphrenic space by the transpleural route, through which an abscess was drained. The primary abdominal wound continued to drain profusely. Later, symptoms and signs of acute ileus were observed. A barium enema disclosed a point of obstruction proximal to the ileo-cecal valve. The patient's condition was too grave to do an enterostomy and it was decided to pass a Levine tube to the duodenum with the feeling that it would result in decompression, just as an enterostomy relieves distention. The drainage material was collected and given to the patient by proctoclysis in quantities of 180 c.c. every 4 hours. Immediate improvement followed. The author does not make any positive conclusion on the basis of one case but the reader gathers that replacement of lost gastric and intestinal fluids in certain cases of obstructed ileus is recommended.

Samuel Morrison.

LIEBER, MARSHALL M., AND STEWART, HAROLD L.

"Hepatic and Bile Duct Changes from Obstruction of the Common Bile Duct Due to Pancreatic Carcinoma." Arch. Path., 17:362-380, March 1934.

Twenty-four cases of obstruction of the common bile duct due to carcinoma of the pancreas are presented to show that cirrhosis may develop from non-infectious biliary stasis.

Secretory stasis, dilatation of ducts, vascular disturbances from collateral pressure, and parenchymal atrophy occur, with tremendous volumetric increase in the channels of the biliary conducting system. Venous strangulation and hepatic anemia result.

Bile pigment in the form of granules or droplets may be found in varying amounts, chiefly in the cells of the central portions of the lobule. Regressive lesions are present as mild and localized degenerative and necrotic changes involving the hepatic cells about the central vein, as non-pigmented focal mid-zonal areas of necrosis, and as deeply pigmented biliary necroses occurring either in the outer portion of the lobule or within the portal radicle. A new formation of connective tissue occurs simultaneously with the changes in the bile ducts until after the second month, when a rapid, independent and progressive proliferation takes place, resulting in a well marked deposit of connective tissue. This is interlobular, intralobular, and perilobular in distribution. The hepatic lobules show a corresponding reduction in size, with atrophy at the periphery. The liver possesses little or no regenerative ability in the face of total stasis.

James I. Baltz.

WEISER, H. B., AND GRAY, GEORGE R.

"Mechanism of the Formation of Pure Cholesterol Gallstones." Arch. Path., 17:1-9, January 1934.

Stones formed in the gallbladder in the absence of infection are usually designated as "pure cholesterol stones." The authors have made experimental observations which furnish the basis of a mechanism to account for the formation of such concretions. Their experiments indicate that the presence of a small amount of fat in the bile is most important. Fat acts both as a collecting agent for the particles of precipitated cholesterol, and as a solvent responsible for the growth of the interlacing, needle-like cholesterol crystals into a concretion. This occurs when cholesterol separates from a supersaturated solution in fat.

Pure cholesterol stones, simulating the natural concretions both in macroscopic and microscopic appearance and properties, were synthesized in these in vitro experiments. Olive oil was emulsified by the addition of bile salts, and a supersaturated solution of cholesterol in fat was then added and the mixture shaken. The excess cholesterol particles were seen to adhere to the surface of the emulsified droplets of fat. When a trace of acid was added, to convert the bile salt or emulsifying film (sodium glycocholate) into bile acid (glycocholic acid), which is not an emulsifying agent for fat, the particles of cholesterol immediately came into direct contact with the fat, and went into solution. In a few hours, the cholesterol precipitated out in the characteristic, interlacing, needle-like cholesterol crystals, which formed typical calculi.

Liver bile, after entering the gallbladder loses its alkaline reaction, according to the authors, and develops an acid pH. They state that this change of pH is probably accentuated in the presence of gallbladder stasis. Moreover, normal bile contains fat, and may contain more than 1%. The essential conditions reproduced in these in vitro experiments are, therefore, known to exist in vivo. This fact affords plausibility to the above explanation. The theories of other workers who have attempted to explain the mechanism of formation of this type of calculus are also presented and discussed by the authors.

John G. Mateer.

WILLIAMS, B. W., AND BOGGON, R. H.

Mechanics of Appendicitis. Lancet 226, 9-10, Jan. 6, 1934.

In an analysis of 108 acute and 340 chronic appendices, to test the theory that appendicitis is due to obstruction, it was found that in 97.2 per cent of the acute appendices there was definite evidence of obstruction to the lumen of the appendix. In each case the area of obstruction was found to correspond to an area of thickening and fibrosis of the submucous layer with a diminution of the lymphoid tissue. This area was invaded by cells of a chronic inflammatory type in contrast with the distal obstructed portion where acute inflammatory cells were constantly present. The muscle wall was never involved. The mucous membrane in the strictured area was normal or atrophied. Of the 340 cases of chronic appendicitis there was a history of definite attacks in 38 cases. In all these cases submucous fibrosis could be demonstrated. Of the remaining 302 cases many showed pathological lesions, and as a rule doubt in the finding of fibrosis in the appendix coincided with a dubious history of previous attacks of appendicitis.

From the above observations it would appear that appendicitis, whether acute or recurrent, is almost invariably associated with the presence of a fibrotic stricture in the submucosa. Anatomically, the preponderance of lymphoid tissue in the appendix wall and narrowness of the lumen would explain the difference in the consequence of fibrosis in the lymphoid follicles of the appendix and those of other parts of the intestines.

J. J. Day.

EDWARDS, H. C.

Diverticula of the Duodenum and Jejunum. Lancet, 226, Jan. 27, 1934.

Diverticula may be classified as congenital and acquired. This paper is confined to acquired diverticula of the duodenum and jejunum. A primary acquired diverticulum of the duodenum is a thin walled sac opening from the concave surface of the bowel in the majority of cases around the opening of the bile ducts in the second part of the duodenum. The fundus of the sac is devoid of a true muscle coat. Of forty-two cases, thirty-three occurred in the second part of the duodenum and nine in the third part. The further from the pylorus the less frequently are primary acquired diverticula found. In twelve cases of hernial diverticula of the jejunum five are multiple and seven are single. The pouches vary from the size of a split pea to that of a chestnut and are all situated at or near the mesenteric border. The point of origin of each pouch corresponds with the penetration of the bowel wall by a blood vessel. These pouches must be regarded as herniations of the mucous membrane of the bowel through the muscle coat at points of anatomical weakness; in this case the point of weakness was afforded by the passage of the blood vessels while in the case of the duodenal diverticula the entrance of the bile and pancreatic ducts afforded the point of weakness. The means by which the pressure inside the bowel is raised sufficiently to cause the rupture has not yet been shown, although there is some evidence that in the jejunum irregularity in the contraction of the muscle coat may be responsible. Clinically the symptoms of duodenal diverticula are those of a flatulent dyspepsia or definite pain after meals. Jejunal diverticula rarely give rise to symptoms.

Both can only be diagnosed by X-ray. The treatment of both is surgical. Of secondary diverticula the most important is that associated with ulcer of the duodenum. They are shallow and wide mouthed. Traction diverticula are associated with an adherent gall bladder and are probably of little significance.

J. J. Day.

MOERSCH, HERMAN J., M. D., AND JUDD, E. STARR, M. D.

Diagnosis and Treatment of Pharyngo-Esophageal Diverticulum. Surgery, Gynecology & Obstetrics, Vol. LVIII, No. 4, April 1934; pages 781-785.

The authors report a series of 276 patients with pharyngo-esophageal diverticula of whom 176 were operated upon.

These diverticula should be properly called pharyngeal pulsion diverticula. *They arise on the posterior wall of the pharynx just above* the pharyngo-esophageal juncture (just above the crico-pharyngeus muscle.)

They are more common in men than in women with a ratio of 4.5+:1.

Etiology: Many theories have been advanced. Jackson suggests the lesion is due to the inco-ordination of the crico-pharyngeal pinch cock, resulting in failure to open the upper end of the esophagus.

The possibility of an embryonic or developmental anomaly is mentioned. Judd has noted that dimpling ordinarily appears in the mucosa at the point where pulsion diverticulum occurs. It is conceivable that such a dimpling in these cases is more marked and assumes the form of a very small pouch, thus furnishing the proper *anlage* for the development of the diverticulum. Now added to this the inco-ordination of the crico-pharyngeus muscle, causing increased intra-pharyngeal pressure, decreased elasticity of the tissues with increasing age, and the constant accumulation of material in the pouch would facilitate its development.

The symptoms are characteristic, consisting of dysphagia, regurgitation and the production of typical gurgling noises on eating, speaking, or pressure over the sac when it is distended with air or food. It may produce hoarseness and cough due to pressure on the recurrent laryngeal nerve.

The diagnosis is made relatively easy by means of a roentgenological examination, altho' other pathology in the esophagus must be looked for such as, high carcinomatous obstruction of the esophagus, cardiospasm or benign structures. In one case the mucous membrane of the sac had undergone carcinomatous change.

The treatment is surgical and the authors recommend the two stage operation.

Charles T. Sturgeon.

McEVERS, ALBERT E., M. D.

Conservative Treatment of Acute Duodenal Fistula. Surgery, Gynecology & Obstetrics, Volume LVIII, April 1934, pages 786-790.

The author cites a case of acute perforated duodenal ulcer which he treated in the usual manner, after which he performed primary Witzel type jejunostomy. On the fourth post-operative day a duodenal fistula developed. Conservative treatment was begun using the usual supportive measures of intravenous saline and glucose. The skin was protected with zinc oxide and kaolin powder, reliquefied recolac was given through a jejunostomy tube and the patient was also fed by mouth using six ounces every two hours for eight doses daily. Some of this mild powder solution presented itself at the fistulous opening. The wound was left exposed to the rays and heat of a therapeutic light about three hours twice daily. The fistulous opening was strapped tightly with sterile adhesive. On the 9th post-operative day there were approximately two liters of duodenal drainage per day. By the 19th post-operative day there was no further drainage and on the 34th post-operative day the patient was discharged with the wounds all healed.

The author feels that a well functioning jejunostomy, done at the

time of the primary operation, becomes invaluable should there develop a duodenal fistula.

Extensive surgical procedures are contra-indicated for the treatment of duodenal fistulae, because of the high mortality rate.

The conservative medical management of a case of duodenal fistula as cited by the author is essentially an attempt to buffer the proteolytic action of duodenal secretion before it leaves the duodenum rather than attempt to counteract the intensive pancreatic juice activity after it has bathed the skin. The author noted that with buffer solution of recolac given by mouth at frequent intervals will dilute and thicken the duodenal secretion, thus rendering that secretion less innocuous to the abdominal wall as well as to the fistulous tract.

Charles T. Sturgeon.

EDWARDS, H. C.

Diverticula of the Colon and Vermiform Appendix. Lancet 226. Feb. 3, 1934, 221-227.

This paper is confined to acquired primary or hernial type of diverticulum of the colon and vermiform appendix. In 621 barium enema X-ray examinations, diverticula of the colon were found in 55 cases. The general incidence is about 5 per cent and occurs in people around 45 years of age. Pathologically a typical uncomplicated diverticulum of the large bowel is a hemispherical swelling on the peritoneal aspect of the bowel. They are always multiple and the commonest site is the sigmoid colon. The sites of election for the diverticula are in two rows immediately to the mesenteric side of the two lateral taenia. These points correspond exactly with the points of penetration of the blood vessels. Microscopically, the diverticula are herniations of the mucous membrane through a gap in the musculature. The diverticula are the outcome not of atonicity but of spasticity of the circular muscle fibers, thus there are areas which are in prolonged spasm with adjacent areas which are relaxed. It is through these latter areas that the herniations occur, at points anatomically weakened by the passage of blood vessels. Radiologically one first sees pinhead elevations, then the saw-edge outline, then a series of flask-shaped protuberances, and in the advanced stages the diverticula are almost complete spheres attached to the bowel by a long stalk.

The treatment of the diverticula is essentially the prevention of retention of fecal matter. This consists in obtaining regularity of bowel movement and the avoidance of excessive roughage in the diet. In mild diverticulitis a washout (small in amount and under low pressure) is of great value. Diverticula of the vermiform appendix were found in 8 out of 1193 appendices. They were of two types (1) those secondary to chronic inflammation and (2) those whose formation preceded inflammatory changes. The point of election was not exclusively the point of penetration of the blood vessels. The mechanism was again considered to be due to aberrant action of the muscle coat.

J. J. Day.

EASTON M. E. AND WATSON, W. J.

Analysis of 100 Complicated Cases of Acute Appendicitis. Surgery, Gynecology & Obstetrics—Volume LVIII, April, 1934, page 762.

The authors studied 100 cases of acute appendicitis—records of the Knickerbocker Hospital, New Britain, Conn., during a period of between January 1931 and July 1933.

They call attention to the high mortality from acute appendicitis. It is interesting to note that vital statistics for 1929 show deaths from appendicitis as 15.2 per 100,000 population as compared with 11.8 in 1919 and 9.7 in 1900. The question must arise here however, as to whether such mortality figures are not affected somewhat on the more accurate diagnosis of acute appendicitis in 1929 as compared with 1900 thus producing the increase in mortality. Many physicians will recall the early 20th century period with the innumerable cases of deaths from "inflammation of the bowel" that were no doubt appendicitis. In any case the mortality of appendicitis is most assuredly too high. The concensus of opinion is that this high death rate is due chiefly to indiscriminate use of purgatives by the laity, to delayed operation and to imperfections in operative technique.

The author's series were patients who have had seriously complicated acute appendicitis, *namely—gangrene, abscess, perforation* or diffuse peritonitis. In 42% of these complicated cases there was a positive statement of pre-operative catharsis and six of the twelve who died had taken a purgative.

The author calls attention to the value of enterostomy as a life-saving measure in selected cases of extreme severity and also to the fact that such enterostomy is more likely to prove successful if done at the time of primary operation rather than later on. They consider that primary cecostomy or enterostomy prevents the onset of paralytic ileus and that if the operator plans to drain the bowel, such procedure should be done at the time of primary operation.

Wilkie states that cecostomy is unquestionably indicated if at operation a grossly distended caecum is found. It seems well worth emphasis to say that propyhlatic surgery in performing early enterostomy to prevent ileus in severe cases of appendicitis is worth far more than the usually worthless "gesture" of draining the paralyzed atonic dilated bowel after ileus has developed.

Charles T. Sturgeon.

WILKIE, D. P. D.

Jejunal Ulcer, Annals of Surgery, Volume 99, March, 1934, Number 3, pages 401-409.

The author calls our attention to the fact that jejunal ulcer is a real if somewhat melancholy interest to the surgeon. Jejunal ulcer is more common in men than in women and more common after gastroenterostomy for duodenal ulcer than for gastric ulcer, also more frequent among the Teutonic and Semitic races than among those of Anglo-Saxon stock. It occurs more frequently in patients who before operation had a high gastric acidity and little gastric retention and it occurs but rarely in patients with old standing pyloric or duodenal stenosis and with low gastric acidity. Incidence is variously stated at from 2 to 40%. The author's own incidence of recurrence is 3.5%.

Prevention:

1. In all cases of duodenal ulcer with high acidity and little or no stenosis, he avoids doing a gastroenterostomy and performs either a gastroduodenostomy or some form of plastic operation at the pylorus.

2. As infection is another factor in the etiology, the eradication of septic foci—the teeth, tonsils, appendix and gall bladder, should form an essential part of therapy.

3. Injudicious or heavy handed use of clamp during operation may determine an area of lowered vitality.

Gastroenterostomy should be regarded not as a cure but as an incident in the treatment of peptic ulcer.

Complications:

As part of persistent dyspepsia, the following may occur:

1. Recurring hemorrhage most common and most difficult to treat. Blood transfusions and then surgery.

2. Perforation into the free peritoneal cavity is not uncommon. Difficult to close without narrowing the gastrojejunal outlet.

3. Subacute perforation—an inflammatory mass develops to the left of the umbilicus. Conservative treatment must be followed until the inflammation has subsided. If local conditions permit, the region of the anastamosis must be freed and a partial gastric resection performed. If the condition of the patient is poor and inflammatory infiltration of the mesocolon and root of the mesentery is such to present obstacles to resection, reasonably good results have followed double short circuiting operation—gastroduodenostomy to exclude the old ulcer and a duodenojejunostomy to exclude the region of the jejunal ulcer.

4. Secondary duodenal ileus may occur. Tendency to thickening and fibrosis in the region of the stoma leads to narrowing and in some cases almost occlusion of stoma. Drainage of the duodenum is necessary if complete relief is to be gained by establishment of a duodenojejunostomy. In some cases this operation must be associated with direct attack on the jejunal ulcer and the original stoma.

5. Jejunocolic or a gastrojejunocolic fistula.

a. Always of grave import.

b. The regurgitation of fecal matter into the stomach destroys all appetite for food and leads to characteristic anemia.

c. The entry of partially digested food into the colon causes persistent diarrhea and loss of weight.

The region of the fistula is found engorged and edematous. The lymph vessels leading from it are infected and a clean resection is well nigh impossible.

The one stage operation carries the high mortality of almost 40%.

If the patient's condition is good and the fistula is small, freeing and closing the colon and dealing with the jejunum by resection and possibly followed by a partial gastric resection may be feasible.

In the majority of patients the condition is grave, therefore the author recommends a two stage operation. By excluding the portion of the colon involved in the fistula and allowing a period of some weeks or months to elapse, a relatively clean field can be obtained for the second and major stage of the operation.

Charles T. Sturgeon.

SECTION VIII—*Editorial*

The editorial contributions published in this Journal represent only the opinions of their writers. Such being the case, this Journal is in no way responsible for editorial expressions.

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

THE PROMPT DESSEMINATION OF MEDICAL KNOWLEDGE

Recently, when reading a well-known medical journal, we observed that, of eleven major contributions, seven had been delivered at important national or regional congresses a minimum of seven and a maximum of thirteen months prior to their being printed and thus being made available to the general medical profession.

A not-so-long-ago published book was in process of compilation and "in press" nearly one and three-fourths years. The material comprising the sections written by a group of authors had been "brought down to date" from magazine literature printed during the two years prior to the compilations constituting the several sections of this "new" book. Obviously, it is apparent that, with all the system, diligence and skill capable of being exhibited by modern publishing houses, by the time a volume is placed on sale, much of its contents already is more than slightly mildewed; a considerable amount has been supplanted by recent researches, practices and procedures.

Even in the case of those "systems" which, by the periodic issuance of "new leaves for old" strive *via* the agency of professional and lay writers, or "hacks," to rush "the very latest" to the firing-line of practice, the mechanics of compilation, type-setting, printing and distributing demand months, though the teamwork may be excellent and the object laudable. Moreover, it is common knowledge that few indeed of the "loose-leaf systems" are so constructed that the volumes conveniently may be handled or read. There has not been devised any type of binder which permits such volume of constantly-varying, page-number being read without one's attention becoming split by the gadgets which have to do with locking up the separate leaves. Personally, never have we had the pleasure of possessing or seeing any "loose-leaf system" whose trick make-up allowed the volume to lie open and flat upon a table or stand, thereby permitting restful perusal of a flat book or easy reading of right or left-hand page at its binding-edge or of note-taking. Valuable though these ever-refreshed "systems" may be—as indeed they are, compared with the antiquity of the average text-book by the time it reaches the ultimate consumer,—it would seem that there is a great opportunity for the exercise of real ingenuity in the devising of binders which are practical and annoyance-free. Perhaps, when an actual reader, (not a mechanic) who is endowed with a keen inventive bent, attacks the binder-problem, a perusable book and not a *box*, filled with slipping leaves, will emerge. But the resourcefulness and patience of a Henry Plummer must needs be available before the existing limitations are overcome. Unfortunately, Dr. Plummer not yet has found time or humor for the task and no one, with similar many-angled view or his degree of technical wizardry, yet has appeared.

But, we digress from our main thesis—namely, that our quickly-moving medical world cannot afford to wait months or even years until there are brought to the profession important scientific truths, clinical procedures, advances in therapy or technique or the notice of inaccuracies or inconsistencies of methods long considered reliable or standard. Few physicians there are, particularly in these days of flat purses, who find it possible regularly to visit clinics or to attend useful conferences. Hence, it is evident that the mass of our profession still must depend upon the printed word, be it in magazines or in books: all too frequently by the time theses are available, the subject-matter is incomplete or *passe*. Witness the archaic "knowledge" in respect pathology, diagnosis and therapy upon amebiasis accessible to the general man in so-called "modern" text-books. Or again, even after more than ten years of surgical, roentgenological and pathological investigation, "peptic" gastric ulcer, the damage it produces and its management, still occupy many pages in the most widely circulated text on Internal Medicine, whereas discussion of the four times more frequent, duodenal ulcer, rarely is granted as much as one page! Cardiospasm, the most frequent cause of dysphagia, is given a few lines: ulcerative disease of the small and the large bowels is scantily and vaguely discussed; dyspepsia, fundamentally dependent upon allergy, is dismissed with few and halting words, but "digestive neuroses," elaborately are detailed from a score of angles: in fact that classification becomes the scrap basket into which are cast all dyspepsias with whose etiology, pathology, clinical manifestations and treatment the authors are unfamiliar.

True it is, that a specialist in digestive diseases and nutrition should be, first, an internist. Also it is true, that one whose daily practice and routine reading include 90% of lung-heart-kidney anomalies, should not preen himself upon being the possessor of an amount of special knowledge in below-the-diaphragm-ailments equal to that which he has accumulated in disturbances of the lungs and the cardio-vascular-renal system. Yet any hospital "rounds" will demonstrate how frequently the heart-lung-nephritician is treating ulcerative enteritis or colitis, biliary tract and liver ailments or duodenal and gastric ulcer, "on general principles"—the basis of which management rests upon diets set forth in various decade-old (or longer) "standard" text books or the "latest" contributions in two or three "accepted" medical journals, such contributions being a year or more old when they were absorbed by the general internist as his *vade mecum*.

Radio instruction holds possibilities but *there* the problem lies in eliminating the lay listener: thus far, "selective," group-to-group broadcasting is not available.

In no field of endeavor is knowledge—investigative, pathologic, clinical, therapeutic—advancing more swiftly and certainly, than in that concerning lesions of the digestive system or of nutrition. "Established entities"—peptic ulcer, gall bladder disease (so-called), colitis, oesophageal lesions—are not "established" and the "entities" rapidly are being subdivided into affections not alone specific as to location but, perhaps, specific as to cause. No more impressive demonstration is possible than is the modern conception of ulcerative colitis—a subject concerning which the data in texts so recent as one year, justly should be consigned to the waste basket. And now, thanks to Crohn and his associates, Harris, Bell and Brunn and Corr and Boeck, ulcerative lesions of the small intestine appear as ailments demanding most serious attention. It is to affections such as these non-tuberculous bowel ailments that special consideration be given—and *immedialely*. One may not wait a year or two

before their existence and their actual or potential damage is appraised by the issuance in journals of papers long ago read, the ink on whose manuscripts has faded as they lay in editorial *sancta* or until compilers of books get around to considering them in fat, expensive volumes. The afflicted are in our practices, they demand recognition and care *now* if chronic disablement, economic inefficiency or *exitus* is to be prevented.

This Journal has recognized the necessity for the early printing of worth-while contributions in its field. It aims—and will continue so to do—at promptly publishing, fully and completely, purely scientific investigations and clinical studies which are real advances or are reliable summaries of existing knowledge on timely topics. Perusal of the Journal's index for its first quarter-year discloses the faithfulness to which this policy has been adhered. It has brought to its readers valuable and authentic contributions upon amebiasis, allergy, biliary-tract affections, chronic ulcerative colitis, "regional ileitis" (Crohn), probably better termed "chronic ulcerative enteritis," Von Bergmann's "hiatus syndrome," diverticulosis and diverticulitis, rectal cancer, roentgen evidence in acute abdominal affections, X-ray effects upon gastric juice secretion and composition, important researches in primary anemia, gastric secretion, gall-bladder emptying, besides presenting abstracts of significant advances appearing in publications other than this. Unquestionably, much of what already has appeared in the columns of this Journal will not be printed in text-books within a year—if so early.

This policy of diffusing genuine advances in research, in clinical practice, in technique, will be maintained. How well it is being carried out can be noted by observing, in connection with each contribution, the date on which that article was submitted for publication. Rarely will one discover that any manuscript has lingered longer than sixty days in the editor's office; many do not remain so long. Monthly, there will be available to readers the best efforts from the laboratories, dispensaries and clinics of this Continent's most reputable authorities.

So soon as submitted manuscripts have been read and approved by special and competent groups from the Editorial Council, they will be edited and forwarded to the publishers. This may mean a variation in the size of each Journal issued, but, provided material is promptly in the hands of subscribers for their sight and use, what matters it if one issue contains 30,000 words and another 100,000? Our policy does not include the doling out to readers of a set number of pages of printing, irrespective of quality, at certain cycles in the moon's and the earth's orbits.

It is this policy to which we have pledged ourselves. We believe that only such plan of action is fair and just alike to authors and to readers.

F. S.

MEDICINE: A PROFESSION, TRADE OR TENT-SHOW?

"*DIET DERBY*"*

"Three Chicago women, hired for their heft, last week hopped on scales to show what a week's competitive dieting had done for them. In blatant co-operation to teach rumpy Chicagoans how to reduce were Dr. Herman Niels Bundesen, President of Chicago's Board of Health; Dr. William I. Fishbein[1], able young brother of the American Medical Association's Dr. Morris Fishbein, and William Randolph Hearst. Mr. Hearst's Chicago Herald & Examiner, which hired the women[2] because their chunky thighs and beefy arms would photograph well, instigated and made great ado over bananas.

Two bananas and a glass of skimmed milk was all the nourishment that Alice Joy received at any meal. Drs. Bundesen and Fishbein also allowed her some coffee and tea (without sugar or cream) and large quantities of water. A week of that diet lost her 4½ pounds, brought her down to 135¾ pounds, made her whimper: "I'm hungry. And I'm tired. I couldn't lick a kitten."

Felicia Terry followed the same diet, plus a bit of liver at dinner, and fell from 165 pounds to 162 pounds.

The third woman, Deon Craddock, followed a mixed diet of cereals, eggs, potatoes, vegetables and ice cream ranging between 1,100 and 1,200 calories per day. After a week she had reduced 2⅜ pounds to 142⅛ pounds.[3]

The three expect to continue their "diet derby" until the month's end.

But they are not altogether happy about the springtime sideshow they are providing for Chicago. Dr. Fishbein gave a lugubrious interview about their glands. Dr. Bundesen was making them believe themselves larded with excess blood vessels. Said he last week to the Herald & Examiner: "Each pound of fat contains 4,500 feet of blood vessels. So a person 30 pounds overweight has 25 miles of extra blood vessels."

Well, ain't nature grand?

Our editorial duty is very plain—we do not approve of such popularized methods of teaching the public how to reduce the body weight. Seriously, there is a time and a method, peculiar to each patient, and the decision ought to be left to the practitioner. We do not approve, either, of introducing physiological speculations to the science-hungry laity. We might champion the inalienable right of the average citizen to dependable information, or the prerogative of the physician as a standard source of safe advice, but would either the public or the physician care to hear more in such hot weather?

The sponsors of the diet derby must have had lots of fun.

Perhaps in these rainless days, humbly, we might suggest that when the current "Derby" has run its course in the H. & E., the versatile lads conducting it launch a "*Diabetic* Derby" and thus demonstrate their generous instincts towards the welfare of our parched trees, shrubs and wilted perennials. If their reference-library lacks it, we know where can be found the original words of that classic verse dealing so eloquently with the male canine, whose misfortune in being deficient in Langerhans' islet-function, turned out to be the very factor which brought him triumph and eternal fame.

F. S.

*Excerpt from "Time," May 21, 1934, pg. 50.

1. Generally acknowledged "ghost-writer" for Health Department "Prexy" Bundesen's Chicago Daily News Column ("Your Health: How to Keep It"). A graduate of Rush Medical College, 1924; listed with indicated specialty, none; institutional affiliations, none (Chicago Blue Book, 1932).
2. Of course, the dietetic "experts" labor *gratis* and wholly altruistically!
3. What the young damsels *really* think about the "diet" can be learned by visiting a little book-shop just West of *Boul' Mich'* on the near North Side of Chicago! Particularly, should one get their reactions when, supposedly and presumably, *they are broadcasting via radio from Station W.B.B.M.!*

TO THE FAD-BOUND OVERWEIGHT*

Milk, bananas, coffee clear,
Chopped hay, olives, lager beer,
Powdered walnuts, swig o' gin,
Thirty days—then you'll be thin.
Vary this or cut out that,
"Mind o'er matter," when you're fat!
Critic call it what you choose,
C'est toujours le même damn chose!

Blood of snail or horn of toad,
"Overweight" 's a mighty goad;
If you yearn a figure slim
Exercise with steadfast vim;
Steaming towels, Turkish baths,
Turn and twist like circus laths;

*With apologies to the late Bert Lester Taylor, Esq.

Never let yourself be still—
Pay each month's "conditioning" bill.
Critic call it what you choose,
C'est toujours le même damn chose!

Eighteen days this diet eat,
If you want to see your feet
O'er your tummy's bulging globe,
When at night you dare disrobe;
Eighteen days—it may seem years,
Starve to live, and just "play ball!"
Away real cooking—steaks and all!
Clinch your jaw, and your teeth skin,
Must have guts if you'd get thin!
Critic call it what you choose,
C'est toujours le même damn chose!

Bran, hard egg and watercress,
Sour pickles—what a mess!
Luncheon means a jelly-bean,
"A sweet day treat"—don't get *too* lean!
Dinner, once the day's reward,
Now is aspic, weak tea, chard;
Bedtime comes, no ice-box treat,
Aqua dest.—you take it "neat"!
Critic call it what you choose,
C'est toujours le même damn chose!

Crunch with joy a nasty slab:
Gonad extract made in "lab,"
Gotten from ten mangy bitches,
Dirty, breedless, Macbeth's witches;
But you lack that vital spark,
Hence, on you, the lard will park!
"Special" glands by hypodermic—
Costs a fortune, makes you sick,
Critic call it what you choose,
C'est toujours le même damn chose!

"Daily dozen," swim and hike,
"One and two," harsh o'er the "mike,"
As at six you break your sleep,
Numb and weary, fit to weep;
Dance and squirm like ballet-girls,
Throw a flip-flop, now some twirls,
Flat on floor, now sit up straight!
Work it off—let breakfast wait!
Critic call it what you choose,
C'est toujours le même damn chose!

Out at four on Sabbath morn,
Walk ten miles at "Prickly Thorn,"
Whack that ball a double round—
Arches sink, but lose a pound:
At the nineteenth hole you flop—
Water? Rickey? Not a drop!
If you falter, lost you are,
Pounds will gather, scales you'll jar!
Critic call it what you choose,
C'est toujours le même damn chose!

Thus you strive with main and might,
Suffer, starve and thirst and fight,
Lest your waistband fits you snug;
Pals dub you: "reducing bug;"
No more laughter, no more fun,
With the gang you dare not run.
Sunup's torture, Sundown's more,
When you weigh just as before!
Critic call it what you choose,
C'est toujours le même damn chose!

Does earth hold some blessed isle
Where folks *eat* and always smile?
Where to either girls or boys
Sin is not avoirdupois?
If Clydesdale-born, one merely laughs,
If pinto-pony, more ale quaffs?
And each human yelps with glee
When neighbors live right merrily?
To change one's breed just can't be done,
"Rous mit der quacks"—and save your mon,'
Critic call it what you choose,
C'est toujours le même damn chose!

F. S.

CLEVELAND CLINIC MEMBERS PLACED ON EDITORIAL COUNCIL

The readers of the Journal will be greatly interested to learn that, recently, its Editorial Council has been increased by the inclusion of three well-known and active workers at the Cleveland Clinic, Cleveland, Ohio.

The additions to our official family are:

Dr. Charles Lester Hartsock, Associate in Medicine, specializing in clinical gastro-enterology.

Dr. Ernest Perry McCullagh, Head of Section on Endocrinology and Metabolism.

Dr. E. N. Collins, Dept. of Roentgenology: Gastro-Intestinal Service.

The Journal's readers are to be congratulated upon having available the services of these experienced clinical investigators and through them of having access to the rich clinical and scientific material of Dr. Crile's widely known clinic. Before long, readers may expect a series of important contributions from the Cleveland group.

SECTION IX—*Book Reviews*

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

This Journal is not responsible for the opinions, decisions or grouping expressed by reviewers of books or pamphlets. For the guidance of readers, an attempt is made to indicate the relative worth of reviewed material by placing "stars"— in connection with the reviews. The greater the number of "stars," the more agreeably and importantly has the book or pamphlet impressed the reviewer.*

* * * * *Nutrition* by Graham Lusk, Sc. D., M.D., LL.D., Late Professor of Physiology, Cornell University, Medical College, New York City, with a Preface by Dr. E. B. Krumbaar, Editor, and a posthumous Preface by Dr. Eugene F. DuBois. *Clio Medica:* No. 10 of a Series of Primers on the History of Medicine; Paul B. Hoeber, Inc., Publishers, New York City, 1933.

A little, companionable, into-the-pocket-slipping book, clad in bright red! Psychologists tell us that, given free choice, seven of ten normal humans will select red:—an atavistic throw-back, perhaps, to times when men fed only when the chase was successful, when fire was unknown or scarce, when physical triumph was hunger's best sauce and when the rawer the food the greater the feast! Did the publishers deliberately bind Lusk's "Nutrition" in red so that cover and topic be in harmonious attractiveness? One would not question such *finesse* on the part of the learned and understanding Paul Hoeber, Esq.

Perhaps this invasion deep into the frontal-lobe aspects of publishing and printing accounts for the failure of Editors and bibliophilic *impresarios* to provide Lusk's 124-page volume with an explanatory subtitle: certainly the book's given-name is not adequate. "An Historical Review of its Development as a Science," would seem a subtitle due dollar-scant doctors in these financially rewardless days—particularly those practitioners who buy books that they may glean *feeding-formulae* directly applicable to ill people. Probably no other than the late, eminent and progress-forwarding Professor Lusk could have compressed into a hundred and a scant quarter more, small pages so much essential matter concerned with the *advance* of Man's accurate knowledge of food in its relation to humans, their environment and development, and of what reactions food excites when ingested. But, even though the inclusive name, "Clio Medica," for this series of little books, might inform prospective buyers that *historical evolution only* is to be discussed, yet frankly, how many of our clan, whether in great cities or in villages 'way out yonder, recall the classical phrases of prep days? (most likely the man 'way out yonder!) While contributing generously to our profession's cultural appetite, we believe that the House of Hoeber—one of the country's few exponents of aesthetics as applied to medical publications—overlooked an unusual sales-opportunity when it sent forth this "Nutrition," orphaned from general reading, by carrying no explanatory subtitle. Particularly so, since during the past decade, *via* strange and often astonishing channels, the calorie-vitamin-X-factor-roughage-laboratory-lads have sent along their more or less complete researches to doctors who work with sick folks (from necessity or choice) instead of with guinea-pigs, rabbits, dogs and sad-appearing kine.

With this, perhaps hot-weather-inspired "*caveat emptor!*" (aggravated by reminiscences that "Bazaar" *should* have defeated "Cavalcade" in Kentucky's Derby) now we are prepared to say that Lusk, DuBois and Krumbaar have contributed much to our knowledge and pleasure (However, if the last named is using his Preface (pg. V) as a "set-piece" for *all* the volumes of the "Clio" series, we *do* wish that he would correct the typographical error which makes so ru-dici lous the beginning of line 13 and which nearly spoiled the book for us—in fact, the whole Preface gives the impression of having been written by a tired, busy man after harassment by frequent 'phone calls requesting "Just something!")

In spite of an unfortunate and marked degree of deafness and its effect upon his speech-tones, Lusk was a fascinating lecturer, a stimulus of unusual potency to students and associates. Some of these outstanding personal attributes are reflected in the text as he surveys the steps by which Nutrition arose from the simplicity of primitive man's merely satisfying his hunger-urge to the complexity of an intricate, analytic science encompassing the most minute katabolysis and synthesis of *pabulum* itself and the estimation of basic needs—qualitative and quantitative—for proper metabolic harmony.

Unfortunate, indeed, are those who failed to sit under Lusk and so to have had opportunity observing the *back* of the "back to fundamentals" of his mental inquisitiveness. One simple but characteristic illustration: on pg. 4, Lusk attributes the derivation of "chemistry," the word, to *Khemi*, the native name of Egypt—this land-name meaning literally "black earth," so given because, annually, the over-flowing Nile is responsible for the rich alluvial deposits in the level valley through which the river flows. Even modern dictionaries and texts credit the Greek with the root of "chemistry," e.g., *chumeia* "a fusion," "fluid," "extractive," but not especially attributed to such fluid as seeps from the rich, dark earth along the Nile or elsewhere. Here, as in Lusk's personal researches and his lectures and his publications, the key to what this great investigator regarded as *original* effort strikingly is exemplified. In scores of other instances can the acid test be applied to the exactness and scope of Lusk's knowledge, the manifestations of which were so numerous and so brilliantly yet modestly displayed that McCann wrote: "Graham Lusk's lectures provided superb examples of the reasons why the living voice has not given way to the printing-press. There, on the page before us, were the facts tersely marshaled in logical sequence. Through our ears came interpolations of personal anecdotes which made those facts into a sort of *aura* of living beings who discovered them. Lavoisier was our daily companion, as were Carl Voit and Max Rubner, while Magendie and Claude Bernard appeared never less than once a week!" (Du Bois, Preface II, pg. 7-8.

As to the 124-page treatise itself. Though the book concerns "Nutrition," not until pg. 65 (Chapter V of a total of eight chapters) does the Author specifically *mention* "dietetics" and then only to submit a scant four pages devoted chiefly to an historico-classical mention of scurvy, gout and the well-being consequent upon moderation in food and drink. Characteristically, a song cherished by Boerhaave's students ends the chapter.

Preceding this chapter, Lusk has summarized the nutritional peculiarities, needs, environmental limitations, simple studies—but not infrequently either shrewdly or luckily *basic*—of the ancients (Galen and Aretaeus—he who passed along the word "diabetes," a siphon-like flow of water through the body—are the last of these). He has emphasized the

barrenness of the middle-"dark"-ages, (not neglecting to credit Leonardo with a most strikingly modern set of "rules" or better named, "Aphorisms") until Paracelsus came and passed, furiously crying "I may well rejoice that rascals are my enemies; for the truth has no enemies but liars!" The 17th Century Lusk ushered in by noting Von Helmont's discovery of "gas," a discovery which initiated probably the most important series of investigations in the whole realm of the chemistry of body phenomena and, incidentally, of nutritive processes: A rich epoch this, with its "Royal Society" (1615), Kaiserliche Leopoldina Deutsche Akademie der Naturforscher (1650), Preussische Akademie der Wissenschaften (Berlin 1700), and its host of men who "rubbed the lamp of discovery" even tho' oft their bellies were empty and the winds exposed their unbathed bodies;—an outstanding period, since now men worked with a degree of system and could foregather for discussion of their problems: this concerted "push" far outweighed the former lonely—often jealously secret—single effort. Willis, dubiously, is sipping diabetic urine and telling of its sweetness, Lower is transfusing blood. Sanctorino weighs his sweat-loss, the celebrated Pepys is wide-eyed at Hooke's microscope (but treats his own illness by carrying a fresh rabbit's foot in his pocket!), Mayow is discovering oxygen, Sydenham is text-booking gout from personal experience, Glisson (1650) establishing rickets as an entity.

Great as was the 17th Century, its glories were dimmed by progress in the 18th (Chapter IV). Boerhaave, the sturdy Dutchman, a linguist naturally and by his education, was heard as far as China and became clinically so outstanding that the streets of Leyden echoed to the tramp of students from every nation. Czar Peter lay overnight in his houseboat at Boerhaave's dock so as to be "patient No. 1" next morning (so avows Lusk).

Shrewd, too, was he in chemistry and the yet unborn science of "metabolism," for while Von Haller, of Bern, was proclaiming that the body's heat emanated from the heart and the *friction of blood upon blood vessel walls* (!), Boerhaave was enunciating the doctrine that there existed a "vital element" in the air which not alone was life-supporting, but when lacking, death of animals ensued. Not until the arduous, if somewhat blind, researches of Joseph Black, Spallanzani, Cavendish, and that great *duo* of geniuses, Priestly and Lavoisier, had been completed were there available the "gasses," hydrogen and oxygen, from whose basic properties advanced the main discoveries in the chemistry of the body's breaking down and repair. Not until the late nineteenth and the early twentieth centuries saw the advent of "vitamins" did Nutrition, as a laboratory science, receive another so potent a push forwards. One must read Lusk's concentrated summary of the orderly march of events—a superb effort in "boiling down" the efforts of hundreds of men and thousands of experiments to appreciate the relative significance of these epoch-establishing discoveries towards the laboratory conception of human nutritive mechanisms. (Lavoisier's part in the unraveling of the tangled skein which so long defied the isolation of the all-important "inflammable" and "non-inflammable" gasses is not a little emphasized by reproducing the Rockefeller Institute's portrait of the elegant Madam Lavoisier and her handsome consort—altho', in this celebrated portrait, Madam L. does seem a serious distraction to the continuity of thought of *any* scientist and, besides, appears about to grasp with her delicate right hand, a contrivance which, for all the world, resembles an early-model vacuum-cleaner—about which Lusk is discreetly silent! The distinguished French investigator also is shown later in quaint perspective and with what must have been a most distressing intrusion, surrounded by the social-elect—or mayhap they are models from Paris' leading *ateliers*—as he manipulates a giant "Burning Glass." Certainly if Lusk's plan was to stimulate memory of vital steps in the progress of Lavoisier's studies by employing unusual illustrations better to emphasize "an association of ideas," well has he succeeded!

Neat step, quite naturally since the "essential gasses" had been isolated, was the determination of the "burning-up rate" of man's ingested food. Here, again, in the pre-science of calories" and their varying needs, did Lavoisier, doubtless aided by the best of French *chefs*, show the way even though the atmosphere of Paris was heavy with something more inflammable than oxygen. The Communists closed the Academie des Sciences, arrested Lavoisier, the first scientist not alone of France but of the world, and, in May, 1794, cut off, in one second, that head about which Legrange is said to have remarked, "A hundred years will not suffice to produce one like it!" This "the most criminal act of the French Revolution" occurred when Lavoisier was aged but fifty-one. Mob-spirit removed from the world one of its greatest geniuses; there is no proof that in her last two decades of similar national insanity, Russia learned anything from the tragedies of the French upheaval of November, 1793.

Somehow, to the reviewer, the epic character and the romance accompanying the development of nutrition as a science seems to have been lost after page 63 of Lusk's little book. Volta with his sponges in hawks' stomachs, his stunts at artificial fertilization of bitches and his clever experiments to disprove spontaneous generation, does not accelerate our pulses a single beat. Perhaps because there is no accompanying portrait of a lovely Madam Volta! Certainly to Lavoisier's closest rival, the light had fled from science when the Master's head thumped into the basket at the guillotine: Spallanzani took orders as a holy monk—even Lusk seems depressed—but a few words he gives to Beddoes and his "Pneumatic Institute" and to him and Humphrey Davy, tho' they first demonstrated the general anaesthetizing power of nitrous oxide (1800).

Lusk flees into Chapter V and heads it "Dietetics"—a four page interlude dealing with a few quaint conceits of the early Romans, London and its coffee-houses, scurvy in the Channel Fleet and its banishment when lemon juice and vegetables were given to some 2400 sailors, Benjamin Franklin's windy yarn on how comfortable he had lived on a diet of bread and water—a yarn promptly shown to be a bit of Franklinese hokum by Stark, who apparently was as fanatic as are some of our present professional and lay cranks, but he died; our ever-present cracked-pots seem to live forever!—and Cadogan with his gout, wines, beers and good company.

In the 19th century, Lusk once more reverts to the experimenter, taking as his text what it is assumed the dying Marcus Aurelius, cried: "Laboremus"—let us work—but to Lusk the urge calls for work, *in laboratories*. Now, it is the decline of the French and the ascendency of the Germans. Colorimetry with its exact formulae dominate the picture. Animals instead of retorts and test tubes furnish the data with which scientists of different schools of thought bombard each other. "Organic" chemistry opens undreamed-of fields as procedures of precision take the place of rule-of-thumb computations. The synthesis of compounds leads into fascinating realms as Wohler writes to Liebig, "I must tell you that I can make urea without the aid of kidneys or, indeed, of an animal!"

From animal experimentation to human, chemical physiology is but a logical step: "Stoffwechsel" signifies to the Germans "metabolism" and this word, in turn, soon embraces an enormously varied lot of normal and abnormal physico-chemical phenomena observed in both animals and humans—"calories," first having but chemical application rapidly assume significance concerning foods and their nutritive worth—attempts were made accurately to measure all things, even to the speed of nerve impulses! Never had physiologic processes become so chemical and never before had chemistry been considered as so absolutely the measure of all things physiological.

Oft, indeed, the translations preceded the very writing of the text, a condition which led the great Claude Bernard to exclaim, "Do not think that there are *two* physiologies nor *two* chemistries, one for the normal, the other for the abnormal; the *laws* are the same in both cases!" To Bernard we owe such words as "glycogen," "internal secretion"—master words from a master worker, but a worker who performed his most monumental researches in a dirty cellar: one of the greatest men of France whose inability to supply his wife with a horse and carriage, lost him the wife but, perhaps, assured the everlasting fame as a scientist.

Systematic instruction in organic chemistry and its relation to life, growth, specific organ-function and, perhaps—though the pathway not yet was well-defined—nutrition began to appear. We find Liebig (1840) lecturing in England and two years later publishing his famous "Thierschemie." Voit, Bidder and Schmidt, Johannes, Muller, Regnault, Reiset, Pettenkofer—names still to conjure with!—set the pace, as about them gathered hordes of eager students, fascinated with the almost daily revelations of the "new science:" applied organic chemistry, its truths tested by experimentation *in vivo*. "Respiratory quotient," "nitrogen equilibrium," "protein-sparing" foods, "intracellular activity," "basal metabolism" became white stones marking the highway of progress.

Never did scientists work under such "forced draft;" they were "in on the ground floor" and made the most of it! Never has science witnessed such turmoil as dogma and facts clashed! Never were so many facts of prime significance unearthed in so brief a period! This was, indeed, the Golden Age of Science and the period of intellectual giants! What then shall be said of the Modern Phase? Lusk allots it thirteen pages! Of these, five are devoted chiefly to Max Rubner (1854-1932) who, when a youth, visited England and returned to Munich with a Frankland calorimeter, an instrument devised for determining the caloric value of foods. Not a vast equipment to be sure, but in Rubner's hands, it led to the exact estimation of the caloric value of each primary food material: protein, carbohydrate, fat. These observations established the basis for the exact calculation, calorically, of the modern dietary. Next followed Rubner's "law of surface area" and emphasis upon the importance of considering metabolism from the standpoint of *energy*. At once, there was available a system for the study of comparative nutrition.

Not much time elapsed before Zuntz devised a portable apparatus for determining respiratory exchange—"basal metabolism"—in man. By 1893, Magnus-Levy already was busy noting the variations of B.M.R. in patients, well or ill. Lusk, Benedict, DuBois (1912)—and too modestly does the author state it, particularly to those who have not followed closely the science—really established upon a practical, clinical foundation, the now invaluable procedure of estimating metabolism in health and in disease. (Barely more than a page of text does Lusk give to his own notable contributions: certainly, his stature seen in Time's perspective warrants less modest dimensions!) Deeply stamped with Rubner's influence as is the last chapter in Lusk's little book, we of this land can nurture a legitimate pride that, should the honest scientist abroad read the chapter, in all probability, he would not make it Rubner-dominant but Lusk-dominant. Of vitamins, one gets no evaluation. Only in the chapter headed "Dietetics" is this quality of nutrition hinted at. McCollum's work is scarcely more than mentioned. Evidently Lusk felt that what could not be measured accurately still had to earn its place in nutrition and the chemistry thereof.

This last chapter, to a degree even greater than the eulogies of Professor Lusk's associates within Preface II, stamp the man: untiring, scientifically honest, loyal, modest, skilled in his craft, so familiar with the work of others through the centuries that what he accomplished in his own life seemed to him small—yet to others of a quality and volume ranking him with those whom he so delighted to honor and commend. Only Lusk appears to have been unable to make a correct appraisal of Lusk's place in science, particularly into science of Nutrition.

This volume "Nutrition" is a worthy addition to the House of Hoeber's "Clio Medica" series. As are all Hoeber's books it is well-bound, clearly printed, authoritative, adequately indexed and generally attractive. The illustrations are excellent: all distinct and several quite different from the pictures ordinarily inserted in books concerned with purely scientific subjects. A comprehensive bibliography greatly amplifies the volume's usefulness to those of enquiring spirit.

But we do regret that the book bears no subtitle defining its scope.

Frank Smithies.

* * * * *The Vitamins In Health and Disease.* Barnett Sure, Ph.D., Williams & Wilkins, Baltimore, 206 pp., $2.50.

This book possesses the incomparable advantage of being written by an authority on the subject, by one, in fact, who has devoted many years to the practical investigation of this most absorbing and difficult field. The book is not written for medical readers especially and hence there is added considerable exposition of medical terms and much simplification of data which detracts from its charm, but in no way injures the effect of reading it.

The story of how the general consciousness of "accessory food substances" arose and ultimately led, by devious channels of theory and investigation, to our current concept of the vitamins (omit the "e" to be correct) forms a chapter in medicine and in biological science whose glamor and importance never will decrease but always remain as one of the truly romantic passages in scientific history. An added interest arises when it is remembered that most of the experts responsible for this rapidly-nurtured, new science are still alive, that even 20 years ago the whole field was little more than speculation. A famous pharmacologist in 1918 wrote that the effects of cod liver oil could be duplicated by administering any good foods and fat.

One strong impression left upon the reader is that our American diet is lamentably deficient in vitamin B1 and perhaps B2, as well. The argument for this opinion is well proved by the author; and if reading the book does nothing further than to emphasize this point, it is extremely worth while. In practice it can easily be shown what remarkable results frequently can be obtained through the use of vitamin B concentrates in a variety of different conditions, and it seems that, clinically, too little emphasis heretofore has been placed on this aspect of vitamin administration.

All the known vitamins are very clearly described from the standpoints of discovery, distribution, clinical and experimental results, and descriptions of diseases resulting from deficiency in feeding. A strong suggestion is made that vitamin lack is of importance not only in the well recognized syndromes of beri-beri, xerophthalmia, scurvy, rickets, and sterility, but also in a countless number of abnormal physiological states, the identity of which is as yet vague and the symptoms are but irregularly charted.

The chief value of the book is its unusually clear presentation of the modern knowledge of vitamins in a manner that leaves the reader with a much improved general grasp of the subject. It is useful, not alone to the research worker, but also to the practitioner. This volume ought to be added to the library of every gastroenterologist.

Beaumont S. Cornell.

SECTION X—*After "Hours"*

The Gold-Headed Cane



NOTE TO THE READER:

Of necessity, before the now famous Cane can perform his ancient purposes of being the medium through which are reflected the nature, forms, policies, practices and distinctive episodes—for even in our day such may be dramatic, epoch-making and fascinating—of the modern life, medical, a brief review of his origin, position, quality and his cast of mind is demanded. Patience-trying, though such account may be, the Author trusts that, eventually when the plan has unfolded, much of its present vagueness will have disappeared and experiences of an interesting and enjoyable character readily can be forecast.

Certainly, the remarkable chain of circumstances which made it possible for a Gold-Headed Cane, of unusual associations, to leave the famed Library of The Royal College of Physicians, journey to America, there, again, to serve masters of eminence and to participate in events far different from those common to his earlier career, would seem intriguing.

Perhaps an occasional Reader will enjoy a sense of relief in perusing lines not wholly scientific or laden with tales of human discomfort—in which recital the "human" is transformed into a "case," identity lost, a number is affixed, he occupies a "card" and, henceforth, enters the musty realm of "literature," to be tossed from one "bibliography" to another within the covers of existing, nay, even yet unborn, books and magazines. A few, too, there may be who will respect and honor this astonishingly transported Gold-Headed Cane as they were wont to do when former pilgrimages took them to the Library of the New College and when, at the sight of that venerable relic, the roar of London was gone, and in its stead, came delightful visions of an evening session of the scarlet-clad Fellows and the long-stilled voices of Linacre, Sydenham, Hunter, Radcliffe. Some there may be, who will learn to love this mysterious American Gold-Headed Cane for his own virtues and will find pleasure in detailing to the Author episodes in which they themselves occupied a prominence not altogether eclipsed by that of the distinguished traveller from England.

(*SYNOPSIS* of Previous Chapters: In 1688, the eminent Dr. Radcliffe, of London, began to carry a Gold-Headed Cane of unusual design; this Cane became intimately associated with him by his colleagues and the socially select of England. As he approached years of inactivity, Dr. Radcliffe conceived the idea of passing on The Cane to the *confrere* who, in his judgment, was destined to be his professional successor. The first recipient was Dr. Mead. Through him, the succession to The Cane definitely became an established custom: during a period of nearly 100 years, the honor of being the temporary possessor of this much-coveted *insignia* of outstanding worth fell upon Drs. Askew, Pitcairn and Matthew Baillie. At the death of Dr. Baillie (1825) his widow presented the now venerable and prized relic to The Royal College of Physicians. The Governors of this distinguished body carefully preserved this very sceptre of greatness in a small cupboard located in one corner of the noble Library, from which cupboard, from time to time, it was brought forth for the sight of the learned or the curious.

In 1875, August, the peaceful solitude of The Cane was intruded upon by a strange person, who at first, gave the impression that he was a thief attempting to steal The Cane *in order to profit from the fine gold* comprising its head.

As the seeming theft was being perpetrated, The Cane is given opportunity for commenting upon certain unique historical occurrences in its career, his Masters, the Library and its treasures and to detail gossip or fact respecting distinguished individuals whose interests had of significance in the medical profession, science or national affairs. When The Cane approached what appeared to be impending destruction, the narrative changed rapidly from one tinged with lament and apparent tragedy to that of unexpected comedy. Instead of being rushed to destruction by its uncouth captor, The Cane discovered that it is only being prepared for a function commemorating a forgotten epoch of its life in The College Library.)

FURTHER EXPERIENCES

of

The Gold-Headed Cane

ANONYMOUS

WHAT seemed an interminable period, the strapping charman laboured at his task, much, indeed, to my physical inconvenience. Apart from the discomfort produced by the rough rubbing of my malacca staff, that persistent *massage* with the object of bringing to perfection, in a brilliant polish the grain of the unusual and most carefully selected wood, engendered a degree of heat that almost over-

powered me. Even if the nauseating fumes emanating from the disgustingly penetrating fluid soaking the polishing-cloths had not been sufficient to try my strength and my patience to their utmost, the excess warmth upon this unusually hot August morning, brought me to a state where it appeared that consciousness could but remain a brief time longer. However, again it was demonstrated—as oft it is in the lives of members of the human family—that true *stamina* inherently is associated only with generations of high position and quality of ancestry. Thus, when I had succeeded, but by the exercise of the greatest degree of courage (it is hoped that the employment of this word is not considered a careless or self-inflationary boast!) and dogged, teeth-clenching persistency, in maintaining an outward appearance of unruffled calm, he, (whom then it occurred to me, humorously, to regard as my *valet de chambre*), ceased his vigourous ministrations, brick-red of face, dripping with sweat—stale of odour and wholly characteristic of his station—breathing heavily and muttering oaths quite uncomplimentary to those who had assigned him his task. He surveyed the results of his exertions with pardonable pride. And well he might: never, in truth, since my personal appearance had been dependent upon the efforts of Joshua Blivvins, man-of-all-work in the household of the elegant Dr. Mead, had my malacca staff shone so splendidly; even after its final coating with the finest candle-wax, surrounding objects were as sharply reflected as in a *boudoir* mirror! Assuredly, simple though my captor appeared, he possessed, in full degree, the attributes of vigour and of thoroughness; with which qualifications alone, my long life had taught me, certain men may go far.

I had but slight respite: my attendant absented himself only sufficiently long to gulp what must have been at least a quart of ale from a tankard set in a cool angle of his den and then began the annoying task of furbishing my famous golden head. How I prayed to have been in charge of a less thorough and conscientious workman! Smothered and gasping from successively applied water and stinking soap-suds, scrubbings with foul, green paste, plungings into almost anaesthetizing pungent *essence* and, lastly, I was well-nigh suffocated by a whitish powder rubbed in so violently that I feared not alone that the precious and elegantly-graven coats of arms of my former Masters would be effaced, but indeed, for my very life. At length the task seemed completed, but, alas no! With a finely-pointed instrument, the exercise of which caused most exquisite physical torture, *signia* on my gold head must needs be removed—and *was!* When, at length, the application of softest *chamois* produced a sheen even superior to that of a newly-minted sovereign, I was too fatigued to share in the joyous pride with which the labourer exhibited me to the first Custodian who arrived.

For the sun now was well up above the horizon, its heat betokened a trying day and, once again, the daily routine of The College became established as numbers of attendants—yea, even one overly-ambitious scholar!—assumed their well-ordered occupations.

Scarcely had my erstwhile kidnaper completed his arduous task, than there came a message from the Senior Librarian that, without delay, I was to be delivered to his custody. My own extensive experiences with world-affairs through considerably longer than a century of most parlous times, medical and national, convinced me that an event vastly out of the ordinary portended: indeed, from the time of my rude awakening that morning—at an hour when scarcely had Old Sol sleepily cast the clouds from his eyes and leisurely stretched himself above the horizon, fuming and fussing in a manner which warned that, for the disturbance of his slumbers, mere mortals would suffer his burning shafts that day—the very air seemed to be surcharged with an energy suggesting that something of unusual significance impended.

A few last rubbings of my gleaming staff, a few quick passings of the down-soft *chamois* over my now resplendant, golden head and with a sigh indicative of great relief, my early-morning intruder gave me into the keeping of that wheezy, empurpled-faced Custodian who, for nigh unto forty years, had sung my place and virtues to those visitors to the Library who evinced interest in me and my remarkable career.

Not carelessly, or lacking appreciation of my station as had been the manner of my sunrise intruder, did the ancient and friendly Custodian accept me. Oft have I observed that those who have experienced years of association with the arts, the intellectual and finer aspects of life and who have come into contact with those who are learned in their craft and tranquil in disposition, unconsciously assume, in manner and in deed, the pattern of their contacts and their environments. Not wholly requisite is initial education or mental agility to the achievement of outstanding dignity and respect: a certain type of man there be, who appears actually to become saturated with intellectual attributes and with a philosophic *phlegm* from those persons and things about him. Such imprint distinctly is born upon the countenance and revealed in the manner of the man: one recognizes it even though he be among hundreds of his fellows. But then, mayhap it is but a certain type of man whom, although born and reared in lowly station, finds refreshment to a birth-implanted, knowledge-hungry spirit, when placed amid surroundings of science and of culture: hence, he remains decade following decade, faithful, humble, gentle but ever eager in the acquisition of learning. In all my travels—and wide-flung they had been as I accompanied my five distinguished Masters—in no land did it seem that there existed, among the high or the lowly-placed, so real a respect for knowledge and those who possessed it, as among my own countrymen. Nor in lands other than our own small, but compact, island-kingdom, ever did I observe so ardent a desire for the attainment of wisdom and of culture as that exhibited by our people. The very reserve, the soft smoothness of speech, the quality of manner and the respect towards those in authority and position, stamp distinctively the English. If it be true that the great Napoleon remarked that, among all his troops, each soldier carried a Marshal's *baton* in his knapsack, verily, it has seemed to me, when I observed men of the Continent, that the commonor of England lacked but the dress and appurtances of his betters to enable him to move with proper dignity among those whose quality had been determined by the accidents of birth.

Thus, my loyal Custodian: Me, he received with the respect due to my worth and associations. Well I knew that his more than forty years of labour among our folios, relics and *objets d'art*, had been not idle days but that, on occasion, he could discourse as learnedly as could many of those deemed most distinguished upon matters, medical and scientific, and upon the voluminous contents of our shelves.

Up the two flights of broad steps leading to the Library, we passed: to me came the impression that those notables whose elegantly-painted portraits lined the walls, looked down with life-filled interest: not interest in me, alone, I would have it understood, but an interest aroused by the reminiscences surging through the frontal lobes of that distinguished clan, as, at the sight of the Gold-Headed Cane of ancient memory, great days, epoch-making happenings, stirring controversies, fond friendships—nay, even hates which had created history—honours, disappointments and tragedies, became, for the nonce, real and dramatic. This progress to the heights harbouring my natural abode, seemed a procession at which the noblest in English science and medicine paid homage, through my own inert self, to my late, distinguished Masters! Such emotions, too, must have imbued my Custodian (to whom the steep ascent of stairs was, indeed, trying), for, air-hungry though he be, unconsciously, his step grew firmer, his back straighter and a glow of pride suffused his countenance as we mustered in review. How different now were my sensations from those of but a few short hours earlier, when, firm, in the grasp of the kidnaper I had descended to what appeared to foreshadow complete annihilation!

At the great double doors giving upon the Library, awaited the Senior Librarian: thin and bent from years of service, deeply sunken eyes peering through lenses thick as bottle-glass, spare of frame—a very rack from which loosely hung his shiny, well-brushed black garments—and parchment-coloured flesh, drawn as tightly over his knobby skeleton for all the world like the coverings of those treasured, musty volumes with which his life was spent: in him were crystallized those qualities which, it is claimed, characterize the octogenarian, genus *vermes bibleothecus humanus*.

But, today, he whom never had it been my privilege to observe smiling, except perhaps upon those occasions, when accessions of rare and priceless folios were exposed to view, bore upon his countenance unmistakable evidences of supreme pleasure. Not definitely did his expression change to what one might designate a teeth-revealing smirk, but the pale eyes lighted, the thin, anemic lips unmistakably separated and the mouth corners perceptibly were elevated. Those, acute to sound, even might have heard a feeble chuckle. Without doubt, circumstances of unusual significance so thoroughly had stirred the blood of the Senior Librarian!

For many decades afterwards, did I hear recounted—not, of course, without such furbishings and inaccuracies as characterize mouth-to-mouth recitals of great events—that upon the memorable day with which we are concerned, the venerable Senior actually roared with laughter so indecorously that his bellowing resounded throughout the great Hall and reverberated down the stair-well so loudly that all labour ceased. Such astonishing an occurrence in that ordinarily, tomb-quiet edifice, it has been claimed, brought all from their sober tasks: wide eyed and with jaws agape, it has been said, the entire population of The College stood in wonderment, speculating as to whether such unheard-of happening signified that the revered Librarian had been taken suddenly with a cerebral softening—sad penalty to a rumoured wildness in his long past youth!—and at once should the "mad doctors"* be summoned, or whether (as those who had a quaint and romantic conceit maintained), their Senior had but recently received word by swift messenger that his "venture-ship" to far-off Australia, had just come to port, laden with a treasure so huge as to be incalculable. Thus it ever was with rumour and with gossip—

By me, a chief actor on this occasion, despite the tales which accreted about the character of the old Librarian, not a cackle was heard from his withered lips, much less actual laughter. And yet, as year piled on year, that day in August, 1875, a silent man's rarely-given smile, became translated by time into an outburst of boisterous and hilarious mirth, and stamped a scholar to succeeding generations far more deeply than did his vast and varied learnings. How oft does history carry down to us the wrong tale of the attributes of those of its personages sufficiently important to be recorded: in this event, the scholar left not a name for knowledge, but because, he who laboured silently, did but once exhibit pride and pleasure openly, about him had been builded a legend which listed him as either crank or adventurer instead of one with a character, rich in devotion, loyalty and erudition.

Naturally, I had expected that the friendly, rotund and now hard-breathing Custodian would deliver me into the hands of the Senior Librarian so that, again, I might be placed in the corner-closet where, for fifty years, I had reminisced and observed the progressive development of what now is universally regarded as the ranking medical and scientific Library of the world.

But during my few hours' absence, other arrangements had materialized. Now it was that I became aware of the cause of the venerable Senior's uncommon satisfaction. After he had received me from the hands of the Custodian, he paused a moment as if in recollection of the final occasion when my last Master, Dr. Matthew Baillie, had stamped into the Library with me, then turned towards where stood that so life-full marble head of the eminent physician—one who had been his own friend and counsellor even before the doctor had become my Master—and, with what appeared to me, moistened eyes, bowed in respect to that silent sculptured head with a degree of grace not to be anticipated in so old and fragile a man and with a sincerity about which there could be no mistake.

Such manifestations of true courtesy and honour and in so simple but correct form are rarely seen. Our young assistants in the Library no longer live but for the Institution. Indeed, even while engaged upon their duties, in what their elders call, almost sacredly, the "Great Hall," oft have I heard them depart from the discussion of books, of methods for binding, the orderly arrangement of our possessions or of those notables who stole from their hurried hours that they might acquire additional knowledge or enjoy communion with long-departed philosophers, to engage spiritedly, in argument about Lord Derby's horse race, the cricket scores of Lord Hawk, the elder, or the impending match at rugger between the Welch and the Scotch! Withal, I must admit that they kept the Library most orderly, the folios beautifully were embound and (though of this observation I would not wish to be the final arbiter), enquirers came to their books or charts with greater celerity and accuracy than when the flappy-pantalooned, oldsters served. This was an advantage acclaimed by some of our scholars but looked upon with suspicious disfavour by those ancients who still addressed even the Senior Librarian as "my good Lad!"

To certain readers, much of the enjoyable flavour of a visit to the Library consisted in pleasant argument with an attendant of long service and in the polite confusion which filled an hour to be wasted when a four-century-old tome at once could not be located, and even when it was, the reference was in error. Our servitors of forty years or more knew well the eccentricities and the tricks of memory of those members whose active part in science or in medicine had waned, in certain instances, before I had become a dweller in the Library. They were quite familiar with such gentlemen of leisure, means or birth, in whom was engrained the pose or the hobby of appearing before the world as intellectuals. To each, according to his manner, his mentality, his station, wealth or varying quirks, the ancient attendants rendered adequate and individual service. This faithfulness had its reward not only in their continuance of occupation in the Library (often, it must be admitted long after the cerebrum's intercommunicating ganglia had suffered serious losses in cross-fibres), but also materially. For rarely did one of our celebrated "fossil-brains" or our pseudo-scholars pass on to the next world but his will conveyed something of significant value to those of The College, particularly of the Library, who had aided in making old age mean something less annoying than gout, rheumatism, the shaking palsy, the limitations imposed by early, though definite, ataxia—certainly, at that time, in London considered as an eminently respectable ailment of advanced years, despite the treatise of the celebrated Sydenham—dropsy, asthma or being cut, repeatedly, for stone or tapped regularly—as was the distinguished Dr. Macaulay—for huge and socially embarrassing hydrocele.

It is not my intention to convey the impression that our Senior Librarian or all those attendants of his age were doddering in a mental second-childhood or that their chief daily occupations were devoted to senile chatterings with equally decadent members. Far from such! Our then Senior, as were several of his associates, was a person of unusually capable and flexible mentality. In spite of his fragile physique, he could be depended upon for long periods of sustained effort and was recognized as an individual of the widest and most exact knowledge: indeed, it was he, years previous to when the term became the designation of one of England's mightiest scholars and ablest statesmen, that Lord Greville gave the name "Old Books-in-Breeches!" In learning, manners and in faithful devotion, he represented the very flower

*Psychiatrists; alienists.

of the self-developed, understanding, solid, middle-class Englishman.

When his silent tribute to my last Master, Dr. Matthew Baillie, had been given, the Senior Librarian then advanced towards what, to me, was a most recent addition to the Great Hall.

Directly facing the massive double-doors of the entrance, and a dozen paces inward from them, of a truth in the most conspicuous position in the room, had been placed a handsome case builded from exquisitely grained, precious woods. Glass, of a crystal clearness, relieved the wood and closed the case's top. A soft and elegant material lay within and formed a sort of couch.

To my amazement—and I must admit, my unbounded joy—as we reached this beautiful new fixture, I beheld a shining plate of metal equally as fine as that of my own famed golden head. Upon this plate not only was my own quality graven but likewise that of those great physicians with whom I had been in closest companionship for nearly one hundred forty years. An emotion of indescribable depth and gratitude gripped me at these definite evidences before the world of my own distinction, at the sight of the list of my long-departed companions and at the proof that, even though more than eighteen busy decades had passed, those of the highest rank in the membership of The College had deemed fit to celebrate my fiftieth anniversary—my "golden jubilee"—as a resident of the Library, in so appropriate and fitting fashion. No longer would it be my lot to stand tiresomely and isolated in the stuffy, dark, corner-closet seeing the sunlight, the books and glories of our Institution, hearing distinctly the human voice or looking upon the countenances of men, only irregularly—and oft, at long intervals—when curiosity or a lively interest in the great days passed, induced a Custodian to bring me forth for exhibition—a task often performed in surly manner and an occasion not always suitably timed for my own pleasure or convenience.

As may well be imagined, a considerable group by now had surrounded my gentle Senior, a group, to be sure, in which preponderated those attendants who longest had been attached to the Library and who, of course, were most familiar with my distinguished past and with my important place in the Institution's priceless treasures. A dreamy, idealistic lot, perhaps they were, but such characteristics should be rated at their true worth in these days of rapidly dissolving enthusiasm for history's outstanding events and the personages connected with them. Sad I am to confess it, but more than once had I heard younger attendants speak disrespectfully of me as "that old walking stick" and hint, even, that some of our elderly and long durationed assistants were on a par, in usefulness, with me and that the Library greatly would be benefited if a half dozen more corner-closets were builded to which might be relegated some of "the old stick" hindering progress! Once, indeed, such sacrilegious remarks were overheard by a servitor who had passed some sixty years in the employ of The College—for it seems that this venerable man was not so deaf as he gave the impression or as the careless speaker assumed: in fact, this particular old servitor had a type of *facultative* deafness, a quality which, not rarely, he exercised to his own comfort when not wishing to be annoyed by useless questionings. It will be many years before I dismiss from my visual memory the astonished, pained and yet patronizingly sorrowful, expression which, at once, moulded the countenance of that ancient man!

Glancing about him with very evident pride, the Senior Librarian smoothed carefully the soft material which formed the bed, as it were, of the elegant case, then drew from the pocket of his coat, a long tube-like device of flannel down. Into this, he proceeded to insert me until nothing of me was left uncovered but my gleaming, graven, head of gold. Gently, I was placed in the case and there lay in the greatest ease and comfort since it had been my lot to comprise one of the relics of most outstanding distinction in the possession of The College. The lid was closed. Thus, after but a few short but strenuous hours after being so rudely awakened from rest and so early in the morning dragged, with scant courtesy, from my corner-closet by that stalwart kidnaper, I reclined luxuriously. What, to me, was of still greater satisfaction was that from my position, henceforth I should be able to observe all that passed in the Library and to look upon those of eminence and quality who sought the advantages and the solace of that noble Hall.

My clothing gave me the greatest comfort, not alone as protection against draughts or careless handling, but due to an ingenious arrangement, at any time, a sort of cape and cap combined could be drawn over my entire head, thereby enabling me to escape the too glaring light or to indulge in quiet, undisturbed rest. Of a truth, as that most philosophic of books states, my "lines had fallen in pleasant places!"

The events of the morning had proved so strenuous to one approaching the end of his second century of existence, that, even before the group which had surrounded me and witnessed my ultimate placement in an environment suited to my rank in English medicine, I had passed unresisting, into Morpheus' comforting arms.

So trying had been my day's unusual experiences that when I awakened, to my surprise, night had fallen. However, all was not quiet: there was that peculiar orderly confusion which betokened, to one long familiar with the routine of The College, preparations for the opening of an evening session. It should not be necessary to explain with what delightful anticipation I looked forward to such an occasion. For fifty years, locked as I was in my comfortless, dark, corner-closet, sessions of The Royal College of Physicians had meant to me only reverberation of an unseen hubbub, the nature of which I could but surmise. Annoying though it was to have my rest disturbed from before nine in the evening to well past midnight, still more provoking was it to one, who for generations had been in the very centre of the scientific and medical world, to be unable to witness the proceedings or to listen to the discussions emanating from the most notable minds in the scholarly world. More aggravating had such meetings been, when on occasion for a few minutes I had been displayed to distinguished members or guests, had caught a glimpse of the Fellows clad in robes of scarlet—nay, had seen even royalty or men outstanding in statesmanship or in international affairs—then, all too soon, had been stowed away in my corner-closet, not to rest, but with a more than normal curiosity, to endeavor to catch the meaning of those happenings which occurred so near to me, yet always, due to the stout walls of my abode, too distant for accurate or continuous following or appreciation. "Session-nights," indeed, had been tortures which sadly interrupted my otherwise tranquil and philosophic life and which, I fear, had embittered me towards those responsible for taking me from active participation in notable events as the companion of a Master successive to Dr. Baillie and incarcerating me in the Library as a relic. There was, thus, an implication in this that my usefulness had ceased or that I should be rebuked for my past activities and shown that in the modern practice even such professional confidences as one might repose in a cane were not permissible or in good form.

Since his elevation to the Presidency of The College, Sir Henry Halford, Bart, had arranged evening meetings of its Fellows held, at irregular intervals, in the Library—a place most fitting, not alone due to its majestic spaciousness but because the surroundings were of a character to supplement the learned discourses presented. It was Sir Henry's acumen which saw in these sessions an opportunity to combine the different groups engaged in scientific pursuits and in medical practice, hence by eliminating prejudices, to build a more solid body and to enroll in the attendance powerful and outstanding laymen who, should occasion arise, might prove invaluable in the advancement of the causes of investigation and practice.

The meetings, later, were held monthly and served the

purposes anticipated by Sir Henry most admirably. Wisely, too, Dr. Halford, during his Presidency limited the length of the sessions to the hours of nine to eleven in the evening. He saw to it that there were selected for presentation addresses which held interest alike to physicians, scientists and an assemblage of gentlemen whose *forte*, if not training, led it to an appreciation of higher learning, the established and the unwritten rule that there should follow no formal debating upon the addresses—thus avoiding bitter controversies or the windy babblings of those seeking to attract attention or of men whose second childhood meant senseless prattling of wearisome length. Discussions there were, but these were confined largely to the period following the closure of each session, when, gathered in congenial groups or about prominent authorities, the Members partook of their tea or coffee. These gatherings constituted by no means the least interesting portion of the evening. Then it was, that opinions were exchanged, criticisms set forth and, oft indeed, the atmosphere became surcharged perceptibly as minds of unusual acuteness clashed in vigorous debate.

On this, my first evening of actual attendance at a session of The College, you may well conceive the keenness and pleasure with which I anticipated the impending events. As the clock approached the ninth hour, rapidly the Library filled with scarlet-robed Fellows. There was a considerable sprinkling of civilians and, in the choicest position, sat a Prince of the Royal House, chatting easily and informally with gentlemen seated about him: for here, in The College, all distinctions of birth or place were abandoned, except those, which, from established custom, set apart men of ruling blood from such as accidents of birth have not so favoured.

Promptly upon the stroke of nine, the Bedell opened the door of the Apartment of the Censors and, carrying the handsome Mace of silver-gilt (presented to The College by Dr. John Lawson, in 1681), led the procession comprised of the President, the Officers of the College and the Censors into the Library. At the entrance of this distinguished body, the scarlet-clad Fellows and all the lay visitors, even he of Royal blood, in deference arose to their feet. The President, alone, was without robe, a custom of long standing. However, he bore his Staff of Office, the *Caduceus*, a superb *insignia* designed by a past President, Dr. Caius, the Founder of the celebrated College which bears his name at Cambridge University.

Long had I looked forward to seeing this important and venerable Staff or authority of the President of The College—for it had been much commented upon by my Masters on account not alone of its beauty but for its classical significance. As I observed the *Caduceus* under the lights of the Library, I could but confess that Dr. Caius had, indeed, been inspired when he designed it.

By its material,* silver, it conveyed the impression that the President must rule with "gentleness and courtesy, in contrast to those who govern with a rod of iron." The entwining serpents supporting the head of the Staff, implied that he into whose possession lawfully it came should exercise wisdom, tempered with impartial judgment. Upon the head of the Staff were graven the Great Seal of The College, this seal placed thereon being indicative that The College, as an Institution, ever should uphold those qualities which conduce to true learning and unbiased opinion.

The Bedell, with his followers, advanced to the handsome and magnificently carved table which served as a *rostrum* for the President. Upon this table, reposed on a cushion of crimson velvet, edged with a deep fringe of heavy bullion, the priceless embound, famed "Book of Statutes" upon whose cover were embossed in colours, the Arms of The College. Beside this volume and also lying upon the crimson cushion lay the Seal of The College, elegant of design, in of purest gold. Such a collection of precious *insignia* was impressive to behold, especially when it be recalled that, well onto three centuries, had these classically significant gifts of the venerable Caius ever graced a session of The College and their meaning ever guided the policies of that primary-organized Guild of physicians in paths of honour and of fidelity. Is it to be wondered that, as I gazed upon these very foundations of the ethics of practice and recalled the part which they had played in building a noble profession from its early beginnings among barbers, mystics and charletons, my own insignificance came upon me and I shrank back into my flannel robe! *Here*, in truth, was I beholding the roots and the very beginnings of what now had grown not only into a veritable tree of knowledge but an *exemplar* of all that concerned wisdom, science, faith and justice!

Upon his arrival at the *rostrum*, the Bedell escorted the President to his chair, saw him comfortably seated and then gently lay the silver Mace before him in front of the gorgeous crimson cushion, the emblem of honour, *honaris honestamentum*, as Caius quaintly put it. The noble *Caduceus* was at that time placed in a sort of bracket at the edge of the *rostrum*, there to remain during the session as a visible staff portraying not only authority but also the kind of virtue to be upheld by him whom Fortune had elevated to the high office of President.

When the President had become seated, then, on each side of him, took their places the Censors and the lesser Officers. Such were clad in scarlet, this flaming colour being in some instances relieved by velvet hoods of scholarship, of less vivid hue, or by orders and medals of distinction. The audience seated itself.

At once began a subdued murmur betokening extreme curiosity and interest. For, not until the President and his escort had been seated, was it noticed that a guest had been accorded the honour of a place upon the *rostrum* and occupied the place of distinction to the right of the presiding officer. Of his quality, there was no question, for elderly though he was, his manner and bearing alike signified that he was no common guest who had been given a place before that unusually distinctive assemblage as a courtesy accorded through mere friendship. Further, this supposition was supported by observing that the Registrar of The College was making no preparations to read a manuscript, a manuscript which, in fact, the guest had himself taken from an inner pocket of his dress-coat and was slowly scanning. For, at that day, by custom, only the President was at liberty to read an address: those of other orations were presented by the Registrar, whose qualifications for the position not alone meant high rank in The College but also the possession of a voice capable of being heard throughout that great Hall. Likewise, he must have an ability intelligently to enunciate correctly for their proper meaning, various foreign tongues. Particularly was it requisite that the Registrar know well his Latin and his Greek, for even so late as 1875, it was not uncommon that, in emulation of the age of Harvey and of Linacre, certain older Fellows were wont to present their theses in the ancient languages. Moreover, the facility with which one now might travel about Continental Europe had, in recent days, brought before The College men of eminence from distant nations, so that not rarely upon the Registrar fell the arduous task of reading manuscripts from the French, the Italian, the Dutch, the Spanish and on several memorable occasions, even the German and the Russian. So, as it will be at once apparent, the Office of Registrar long since had ceased to be considered a *sinecure*, an office conferred as a friendly or political reward, but rather a position of first importance, filled only with the utmost difficulty and, once filled, rarely passing from its incumbent except as a consequence of his illness or decease.

Not for long were the Fellows and their guests kept in ignorance of the quality and the name of their visitor. As the President arose, promptly the busy murmurings became hushed and the Library became stilled. With rare judgment as to brevity and in the most cordial words, he spoke of the great opportunity which chance had afforded The College

*William Munk, M.D., F.S.A., "The Gold-Headed Cane," 3rd Edition, 1881.

in being able to have as its orator, the outstanding clinician, public benefactor and personage of the neighboring lands of the Celts, Ireland, one to whom not only his native land was indebted and proud to honour but that, by his contributions to the literature of medicine, the whole scientific universe claimed as its teacher, guide and part of itself—"I present to you, Fellows and distinguished Guests, none other than Sir Patrick Corrigan, Bart., of Dublin—and of the World!" With an elegant gesture and bow he seated himself amid a tumult of applause.

It was, indeed, auspicious that at my "first session" at The College, I was permitted to enjoy so memorable an occasion. It is not possible for me to detail the remarkable address delivered by that tall Irishman, whose rugged but handsome countenance became fired with enthusiasm and earnestness as he unfolded, in that soft, smooth, picturesque brogue characteristic even of the gentlemen of his native land, the clinical accompaniments of that disease of the heart, aortic valve leakage, or regurgitation, the study of which to him had been lifelong and whose distinctive peculiarities he had so thoroughly mastered. Not alone did he make so clear the mechanistic faults of the heart's interfered-with action that the veriest tyro could picture the angry backward surgings of blood already discharged into the dilated, embarrassed aorta and the strenuous attempts of the huge muscle of the right ventricle vainly to face a double labour, but by diagrams of rare ingenuity and by pictures (which in themselves warranted a place in the very walls of our College itself), but, in manner most dramatically illustrated, by a model portraying the defect in an injured pumping machine, attached to a length of extremely thin and elastic tubing, he showed the variations in the quality of the pulse-wave—as in a great artery—which had caused such pulse to be styled "Corrigan's pulse" and thus had carried his acuteness of observation, his sense of the mechanics of the circulation and, indeed, his own name to the confines of the world of science of medicine.

So simple was his language, yet so precise in meaning, so ingenious were his models, so attractive and well-chosen were his sketches and so kindly humorous were his interjected remarks, that our distinguished assemblage—never, let it be admitted, over kindly to the profession of Ireland, to its representatives or its Institutions—heard the clock strike eleven as Sir Patrick closed, with scarce a person realizing the hours' passing. Not even the elders of our Fellows had left the room—an uncommon tribute to any orator—and throughout the address never even so much as the scraping of a chair interrupted the flow of eloquence or disturbed the sequence of idead.

Tremendous applause proclaimed the pleasure and enthusiasm of the assemblage as Sir Patrick closed with a few well-chosen and congratulatory compliments to the President and to the College. Despite the strong bonds of custom and the strenuous efforts of the Bedell, there was a rush forward to the *rostrum* of our guests and Fellows in an effort personally to express appreciation to the orator and to survey his models and his illustrations at close range.

Certainly, those who served the tea and the coffee faced a task in distributing the refreshment. Long it was before the buzz of comment and discussion died away and only by beginning to turn out the lights, could the caretakers succeed in emptying the great Hall.

As the Library became darkened and as I settled myself for rest, still fired by the evening's important events, the President passed out the door from the Censor's room. Distinctly I heard him remark to his companions that long after all of them had passed from this earth, history would continue to record what they, themselves, had had the privilege of seeing and of hearing that evening and that Sir Patrick Corrigan would go on down through the ages as one of the world's greatest clinical observers and teachers, little though he might be considered in his day by his own countrymen and in England.

Often, since that evening, I have heard confirmed the truth of the President's prophesy.

(To be continued)

SECTION XI—*Societies, Programs and Proceedings*

A REPORT OF THE COMMITTEE "ON A SURVEY OF THE ENZYME TESTS, AS PERFORMED BY THE MEMBERS OF THE AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION"*

By

A. H. AARON, M.D., Chairman, Buffalo, New York
H. L. BOCKUS, M.D., Philadelphia, Pennsylvania
A. C. IVY, M.D., Chicago, Illinois

In 1932, Doctor Burrill B. Crohn, the then President of the American Gastro-Enterological Association, recognizing the many discrepancies which exist in the methods of analysis for enzymatic concentrations in the secretions of the gastro-intestinal tract, incidence of employment, value of these findings in diagnosis, prognosis, and substitution therapy, appointed a committee composed of the authors of this report in an attempt to bring to the attention of the Association the situation in this problem. With this in mind, the Committee desires to report as follows:

Incidence of Employment

General Use:

(A) 135 questionnaires were sent to the members of the Association.
(B) 83 of these questionnaires were returned to us, and upon these we base our report.
(C) 37 members, of this group of 83, reported that they did not do enzyme tests of any type or character.
(D) 46 members do perform the tests.

Number of Times for which Individual Enzymes were Tested:

(A) Gastric Enzymes:
Rennin by 14 members
Pepsin by 23 members
(B) Duodenal Enzymes:
Trypsin by 27 members
Lipase by 20 members
Amylase by 23 members
(C) Blood Amylase: by 1 member.

The reasons given by 37 members of the Association for not performing Enzyme tests in the secretions of the gastro-intestinal tract:

(A) Methods available at the present time do not yield sufficient critical data.
(B) Intricate, time-consuming nature of tests.
(C) Special equipment required.
(D) Variability of the results.
(E) Slight absolute diagnostic significance.
(F) Lack of substitution therapy when there is an absence or alteration in the character or quantity of these enzymes.

Forty-six members of the Association are performing Enzyme tests in the gastric and duodenal contents; their returns are analyzed as follows:

Gastric Enzymes—Pepsin

An analysis of the reports of 23 members testing the gastric contents for the presence of Pepsin. (Figures indicate the number of members reporting on each item).

Diseases Used in:		*Methods Used.*	
Achylia Gastrica	9	Mett's Tubes	9
Hypochlorhydria	3	Egg Protein Blood Fibrin	1
Achlorhydria	7	Cowgill & Gillman	6
Peptic Ulcer	4	Agar Tubes	1
Blood Dyscrasias	4	Anson & Mirsky	1
Gastritis	1	Fresh Milk	1
Carcinoma of Stomach	2	Incubated Egg White Cubes	1
Sprue	1	Biuret	1

Value:			
Determining factor in Achylia	4	Curiosity and no opinion	3
Absence in Blood Dyscrasias	2	Prognostic	2
Unable to evaluate	2	Ulcer	1
Slight value	8		

Rennin

An analysis of the reports of 14 members testing the gastric contents for the presence of rennin. (Figures indicate the number of members reporting on each item).

Diseases Used in:		*Methods Used:*	
Hypochlorhydria	1	Riegel	10
Achlorhydria	5	Agar Tubes	1
Achylia Gastrica	8	No method designated	3
Blood Dyscrasias	2		
Gastritis	1		
Carcinoma	1		
Doubtful Cases	1		

Value:			
Achylia Gastrica	6	Prognostic	2
Control of Diet	1	Only slight value	4

An Analysis and Discussion of the Methods and Interpretation of the Values in the Determination of the Gastric Enzymes

It is evident that it will be impractical to review all of the methods which have been reported in the literature or even all which are now being employed by the members of the Association for the assay of the enzymes found in the gastric and duodenal contents, so we shall only review some of the methods used for the major enzymes found in the gastric and duodenal contents.

Pepsin

Little difference exists between the numerous qualitative methods for estimating the presence of pepsin. The digestion of washed fibrin or carmin-fibrin (Grutzner) is a widely used classroom experiment.

Mett Method: The Mett method (Hawk, 10th Ed., p. 299) is roughly quantitative. It cannot be used for accurate quantitative comparative work, but is simple and easy to perform. It has been given up by many academic workers.

The Gillman-Cowgill method: The photographic film method. (*J. Biol. Chem.*, 88:743, 1930). The Gillman-Cowgill method yields quite accurate quantitative comparisons, but considerable care and experience are required for trustworthy results. This method is becoming popular.

Other more accurate methods: The viscosity method, the method of determining the non-protein nitrogen produced, and the method of formol titration recently were selected by Northrup (*J. Gen. Physiol.*, 16:41, 1932-33) as yielding the most accurate, convenient and significant results. The viscosity method when gelatin is used as a substrate gives reproducible results, but the significance of this physical change may be questioned. The determination of the non-protein nitrogen formed requires considerable time and labor and the results "cannot be directly interpreted in terms of chemical changes." The formol titration yields results of chemical significance, but it must be carried out with care to obtain reasonably accurate results.

The hemoglobin method of Anson and Mirsky: (*J. Gen. Physiol.*, 16:59, 1932-33). After considerable experience with numerous pepsin methods,

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one of us (A. C. I.) has adopted the method of Anson and Mirsky which was developed in Northrup's laboratory. This method gives reproducible results with different batches of hemoglobin which are quite easily prepared and keep well in the icebox for several months. The reagents are easily prepared and the test may be rapidly and readily performed. This method has the appearance of becoming a standard method, but further trial with it is necessary.

RENNIN

Although the biochemical evidence is quite definitely in favor of the view that rennin is not identical with pepsin, clinical investigation *has not demonstrated that a differential study of pepsin and rennin in the gastric contents is of diagnostic or prognostic value.*

The older commonly employed methods of Leo and Riegel are, of course, qualitative.

As quantitative methods, the methods of Fuld (*Biochem. Zeitschr.*, 4:54, 1907) or of Michaelis and Rothstein (Hawk, 10th, Ed., p. 279) are satisfactory. For academic studies, or clinical investigation, it is preferable to use dried milk powder, or the casein-calcium chloride-phosphate mixture of Holter, (*Biochem. Zeitschr.*, 255:160, 1932; also Andersen, *Biochem. Zeitschr.*, 261-262:99, 1933) as a substrate because the constancy of the substrate is insured (see Waksman and Davison, Enzymes, 1926, p. 198). The viscosity method of Luers and Diem (*Milch wirtschafte, Forsch.*, 2:405, 1925) is probably the most accurate and significant method available at present

To obtain reliable and worthy results, it is not believed to be necessary to employ the viscometric method.

Summarizing, it may be said that very accurate, clearcut and easily performed pepsin and rennin methods are available.

CLINICAL OPINION OF DETERMINATION OF GASTRIC ENZYMES

It is evident that the principal reason for doing the tests for the presence of pepsin and rennin in the gastric contents is to determine whether achylia gastrica exists.

When anacidity is found by ordinary gastric analysis at least a qualitative examination for pepsin or rennin should be made, as not infrequently traces of enzymatic activity will persist in the absence of free acid,

A diagnosis of true achylia gastrica is not justified unless both gastric enzymes and free acid are absent after histamine injection.

Even from our returns it is evident that when 13 out of 22 members are unable to evaluate this finding, there is need for a serious consideration of this part of the enzyme study.

However, it is possible that clinical investigation may reveal in the future that a study of pepsin concentration may be of prognostic value, (recent work of Alvarez and Van Zant). Obviously in clinical investigation, one of the best quantitative methods available at the time should be employed.

DUODENAL ENZYMES—TRYPSIN

An analysis of the reports of 27 members testing the duodenal contents for the presence of trypsin. (Figures indicate the number of members reporting on each item).

Diseases Used in:		*Methods Used:*	
Diabetes	1	Lueders	1
Inanition	2	Agar Tubes	6
Pancreatic Disease	21	Willstader, *et al*	3
Biliary Tract Affections	5	Not specified	4
Duct Obstruction	1	Gross	2
Diarrhoea	4	Egg Albumin	1
Jaundice	1	McClure, *et al*	3
Carcinoma Head of Pan.	1	Mett's Tubes	1
Metabolic Diseases	1	Spencer	1
Colon Affections	2	Casein	3
Cerebro Spinal Syphilis	1	Burrill	1
Sprue	2	Hollander	1
Achylia	1		
Gastro-Intestinal Malignancy	1		

Value:			
Useful Procedure	1	Link in chain of evidence	1
Pancreatic Disease	2	Distinction functional and organic disturbances of Pancreas	1
Patency of Ducts	1	Curiosity	2
Carcinoma, Head of Pancreas	2	Pancreatic Duct obstruction	1
Gall-stones	1	Committee to continue work	1
To explain symptomatology	1	Indefinite	2
Slight value	7	Substitution therapy	1
Not stated	2		
Sprue	3		

AMYLASE

An analysis of the reports of 23 members testing the duodenal contents for the presence of amylase. (Figures indicate the number of members reporting on each item).

Diseases Used in:		*Methods:*	
Diabetes	1	Lueders, *et al*	2
Inanition	2	Agar Tubes	5
Pancreatic Disease	16	Wohlgemuth	8
Biliary Tract Disease	1	Not mentioned	3
Obstruction Pancreatic Ducts	1	Viscometric	1
Diarrhoea	3	Bassler	2
Jaundice	1	Ellman	1
Pancreatic Tumors	1	Blood Amylase	1
No answer	2		
Metabolic	1		
Sprue	2		
Doubtful Gastro-Intestinal Cases	2		
Achylia	1		
Arthritis	1		
Achlorhydria	1		
Steatorrhoea	1		

Value:			
Useful, except in Diabetes	1	Not mentioned	3
Pancreatic Disease, acute	2	Link in chain of evidence	1
Pancro-billiary duct obstruction	4	Doubtful	5
To explain symptomatology	1	Curiosity	1
Slight value	1	Substitution therapy	1
		Committee to continue work	1

LIPASE

An analysis of the reports of 20 members testing the duodenal contents for the presence of lipase. (Figures indicate the number of members reporting on each item).

Diseases Used in:		*Method:*	
Diabetes	1	Lueders	1
Inanition	2	Agar Tubes	3
Pancreatic Disease	10	Not stated	3
Pancro-Biliary Tract Disease	4	Rona	1
Pancro-Biliary Duct Obstruction	1	Myers and Fine	5
Diarrhoea	4	Cherry and Crandell	3
Jaundice	1	Reynolds	1
Not mentioned	2	McClure	1
Colon	2	Hollander	1
Cerebro Spinal Syphilis	1	Milk and Litmus Agar	1
Sprue	2		
Doubtful G. I. Cases	1		
Achylia	1		
Arthritis	1		
Pulmonary and Intestinal Tuberculosis	1		
Gastro-Intestinal Malignancy	1		
Metabolic	1		

Value:			
Useful	1	Carcinoma Head of Pancreas	1
Should help	4	Sprue	1
Demonstrates patency of ducts and pancreatic function	1	No value	1
Carcinoma Head of the Pancreas vs. Gall Stones	1	Curiosity	2
Significant in Pancreas and Biliary Tract Disease	1	Pancreatic Obstruction	1
Very slight	1	Not a determining factor	1
Not stated	1	Substitution therapy	1
		New methods	1
		Link in chain of evidence	1

AN ANALYSIS AND DISCUSSION OF THE METHODS AND INTERPRETATION OF THE VALUES IN THE DETERMINATION OF THE DUODENAL ENZYMES

From the viewpoint of clinical investigation much is yet to be learned from a study of duodenal contents. This field, opened by Einhorn, has not been sufficiently explored to warrant the position that some clinicians have taken, namely, that nothing of diagnostic or prognostic value is to be obtained from an enzymic study of duodenal drainage. Further, it is believed that a number of problems in the field of the abnormal physiology of duodenal contents remains to be elucidated. However, it is a difficult and very tedious field of investigation and one in which it is not easy to predict the practical value of the end results.

LIPASE

The ethyl butyrate method: (Myers and Fine; Todd and Sanford, 1931, Ed., p. 422). The ethyl butyrate method is an esterase method and not a true "lipase" method, although it has been used for a long time by biochemists and physiologists as well as clinicians as a "lipase" method. The emulsified oil methods cited below give true "lipase" or steapsin values.

The Einhorn agar-olive oil emulsion tube. This method is roughly quantitative (*Med. Rec.*, 87:968, 1933.)

Emulsified cotton-seed oil. (McClure, Reynolds and Wetmore, *Arch. Int. Med.*, 27:706, 1921). This is a very good method and easy to perform.

Emulsified olive oil. (Crandall, *Am. J. Physiol.*, 100:266, 1932). This method is similar to that of McClure. The emulsion may be made

by hand with gum acacia, but machine-made emulsions are superior. Such an emulsion may be obtained from the Abbott Laboratories. The emulsion should not be used when there is evidence of "cracking". It will frequently stand up for several months in the ice-box.

Willstatter, et al method. (Hawk, 10th Ed., p. 317). This method also employs an oil emulsion. It is accurate and easy to perform but more materials are required.

Lueders, Bergheim and Behfuss. (*Am. J. Med. Sci.*, 166:535, 1923). This method employs a hand-made olive oil emulsion without buffer. These authors claim that a buffer is not necessary for consistent results. Otherwise it is free from objection.

Thus, we have at hand lipase methods for duodenal contents which are quite accurate and easy to perform.

AMYLASE

The Wohlgemuth method, which has been used so extensively, is only a rough quantitative method when applied to duodenal contents, unless used by a careful chemist and then only after some experience with the method.

The Einhorn starch agar tube method is only roughly quantitative.

The McClure, et al method is a good comparative method, but involves the determination of the reducing sugar formed by the Folin-Wu method. This method could be rendered easier by titrating with Benedict's reagent, which is probably as accurate in view of the quantity of reducing sugar present.

The Lueders, et al method (*Am. J. Med. Sci.*, 166:535, 1923) determines the reducing sugar by titrating with Benedict's reagent, which is much simpler and as accurate in view of the quantity of reducing sugar present. The theoretical objection to this method is that a buffer is not used which they claim is unnecessary.

The Willstatter, et al method determines the reducing sugar formed by hypoiodite titration.

Either of the last three methods yield good comparative quantitative results. All are open to the *theoretical objection* that, since maltase is present in duodenal secretion, the reducing sugar present may be both maltose and glucose, and hence the test is a measure of both amylopsin and maltase. This introduces an error into the calculation since the reducing properties of maltose and glucose are different.

The viscosity method of Davison (*Johns Hopkins Med. Bull.*, 37:281, 1925, *J. Biol. Chem.*, 68:75, 1926) is probably the best method in the hands of a careful and experienced observer, but requires special apparatus.

TRYPSIN

The Mett tube method has been employed but is a rough quantitative method, sodium carbonate solution being used instead of HCl.

The Einhorn hemoglobin-agar tube method is a rough quantitative method.

The Fuld-Gross method (Hawk, 10th Ed., p. 313) is a simple and fairly accurate quantitative method.

The following methods are more accurate:

The Willstatter titration method (Hawk, 10th ed., p. 314) is a relatively simple method, which in the hands of one of us (A.C.I.) has yielded good results. In the case of duodenal contents, the reading of the "N" point requires experience with the method. This method, of course, is based on sound principles.

The Lueders, et al method (*Am. J. Med. Sci.*, 166:535, 1923) utilizes the principle of formol titration. The principle of a buffer and optimum pH is disregarded. The principle of "formol titration," however, is a standard principle.

The McClure, et al method (*Arch. Int. Med.*, 27:706, 1921) is accurate and sound in principle, but it involves the performance of a micro-Kjeldahl Test.

The viscometric method of Northrup (*J. Gen. Physiol.*, 5:353, 1923) is a very good method, but requires special apparatus and careful technique like all viscometric methods.

Attention should be directed to the method of Anson and Mirsky (*J. Gen. Physiol.*, 17:151, 1933) in which trypsin is determined by its action on denatured hemoglobin. This method has not been adapted to duodenal contents, but when adapted, it may possibly result in the most accurate and rapid method yet devised.

Three "systems" of analysis for the major enzymes in duodenal contents have been proposed, namely, the *Einhorn*, *McClure*, and *Lueders*, the names of collaborators and the original proposers of the principles utilized being omitted. The Einhorn "system" is obviously roughly quantitative; the Lueders is more accurate, relatively simple, but may be objected to on theoretical grounds; the McClure is still more accurate, theoretically, but is more complicated and not entirely free of theoretical objection.

In this connection a practical question which logically arises is: Is there a sufficient difference in the methods employed in these "systems" of analysis to conclude that one is better than the other, in view of the normal variations due to dilution and other uncontrollable factors that enter to make the duodenal contents a very complex fluid? This is a question which we believe cannot categorically be answered with the evidence at hand. The only way in which this question can be answered is to actually compare these methods, using normal duodenal contents, and thus ascertain if the differences are of practical significance. (According to our knowledge, such work is not reported in the literature.)

CLINICAL OPINION

One outstanding definite conclusion can be drawn from our returns; the absence of pancreatic enzymes in the duodenal contents reveal an obstructive lesion. This is of great importance.

The diminution of pancreatic enzymes has been reported by careful observers in sprue.

The situation in reference to other conditions warrants the most careful review and co-operative efforts to establish their value as a diagnostic procedure and an indication for substitution therapy.

GENERAL CONCLUSIONS

1. The Committee desires to apologize to the Association for its inability to present actual comparative data on the various methods for *determination of enzyme concentration; it cannot refrain from pointing* out that any person or committee which passes judgment on matters that will be moot for some time to come invites criticism.

2. It is obvious that this survey denotes the existence of unsolved technical difficulties in pancreatic and gastric enzyme analysis, otherwise there would be more unanimity of opinion favoring one system of tests. There is insufficient proof at the present time that we have a system of tests which is sufficiently accurate and simple to be routinely adopted for clinical purposes.

3. One of the striking results of the analysis of the questionnaire is that there is a comparatively small number of men in this country who mention the use of blood and urine ferments in tests for the presence in the blood and urine of altered values in suspected cases of acute pancreatic disease and pancreatic obstruction. These methods apparently are much more universally used in Europe.

4. Another practical question is: Does one obtain better information concerning the normality of intestinal digestion by studying the feces or by analyzing the duodenal drainage? This is another question that cannot be answered categorically with the evidence at hand.

5. It has been suggested that this Committee advise the use of a standardized terminology indicating enzymatic concentrations. We believe that this is impossible at this time until standard methods are used, controls established and normal values arrived at.

6. The fact that many of the members of this Association are not performing the tests should not discourage us, as we believe that this is only an indication that if adequate procedures and accurate normal figures were available these members would be doing the tests.

RECOMMENDATIONS

We believe that a committee should be appointed to carry out the suggested plan, if it meets with the approval of the Association at this meeting.

(A) This Committee shall find ways and means of making a comparative and co-operative study of the various enzyme tests.

(B) The preparation of a method of procedure for the co-operating laboratories and clinicians.

(C) In planning for this survey, the Committee should distribute to co-operating members the following form:

SUGGESTED FORM FOR SECURING DATA:

"It is the desire of this Committee, appointed by the American Gastro-Enterological Association for the study of enzyme activity, to collect a comparison of the results obtained, and the value of the various tests for the ferments.

Therefore, will you in a series of 25 normal individuals do

(1) Gastric Extractions

(2) Duodenal Drainages and analyze them for the enzyme....., according to the method of.....described in.....

In order to maintain comparable results will you please use the following method of collecting your specimens:....., and stimulate the flow of juices by the instillation (injection) of.....

Please mail your conclusions, criticisms and suggested modifications of this test to:

Chairman of the Enzyme Committee."

From an analysis of the material secured by the suggested co-operative plan, as above mentioned, it might be possible to draw the following conclusions:

(1) An acceptable method of testing for gastric and for duodenal enzymes.

(2) The determination of a nomenclature.

(3) The selection of a standard stimulant

(4) Then to advise its use in pathological conditions, after normals have been arrived at.

This, of course, does not interfere with the performance of these tests on pathological conditions at the co-operating member's own desire or discretion.

ACKNOWLEDGMENTS

The Committee desires to express their thanks for the confidence reposed in them by Doctor Crohn in appointing them to attempt to analyze this subject.

To the members of the Association for their willingness to be inflicted with a questionnaire, and the complete manner in which these were filled out and returned to the Committee.

To Doctors Anthony Bassler and C. W. McClure for their kindness in sending us reprints and material concerning their tests.

Doctor H. H. Sabotka, of New York City, for his assistance in the preparation of the questionnaire.

Respectfully submitted,

May 1, 1934. THE COMMITTEE.

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CONTENTS

SECTION I—CLINICAL MEDICINE — *Page*

COMMENSAL AND PARASITIC ENTAMEBA HISTOLYTICA INFESTATION—*Lloyd Arnold, M.D.* - 351
TREATMENT OF PATIENTS WITH FOREIGN BODIES IN THE ESOPHAGUS OR STOMACH—*Porter P. Vinson, M.D. and Karl Deissler, M.D.* - 357
A NEW ASPECT OF MIGRAINE AND CERTAIN RELATED CONDITIONS—*Eugene Foldes, M.D.* - 359
ABSTRACTS - 369

SECTION II—EXPERIMENTAL PHYSIOLOGY

A FURTHER PROOF THAT THE GALL BLADDER EVACUATES VIA THE CYSTIC DUCT—*W. L. Voeglin, M.D., H. Greengard, M.D. and A. C. Ivy, M.D.* - 371
STUDIES ON GASTRIC MOTILITY UNDER LOW OXYGEN PRESSURES—*Edward J. Van Liere, M.S., Ph.D., M.D.* - 373
A STUDY OF THE ABSORPTION OF DEXTROSE AND WATER FROM CHRONIC ISOLATED LOOPS OF THE COLON—*Philip H. Moore, M.D. and G. E. Burgel, Ph.D.* - 376
ABSTRACTS - 383

SECTION III—NUTRITION

SOME OBSERVATIONS ON FOOD ALLERGY—*Warren T. Vaughan, M.D.* - 384
REVISED "ELIMINATION DIETS" FOR THE DIAGNOSIS AND TREATMENT OF FOOD ALLERGY—*Albert H. Rowe, M.D.* - 387
ABSTRACTS - 392

SECTION V—THERAPEUTICS

THE MANAGEMENT OF CHRONIC SPASTIC CONSTIPATION—*Harvey G. Beck* - 393
THE TREATMENT OF PERNICIOUS ANEMIA—*S. M. Goldhamer, M.D. and F. H. Bethell, M.D.* - 398

SECTION VI—ABDOMINAL SURGERY

THE UNCOMMON TUMORS OF THE LARGE INTESTINE—*J. Arnold Bargen, M.D. and Claude F. Dixon, M.D.* - 400
SOME PRINCIPLES IN THE TREATMENT OF SEPTIC CONDITIONS FOLLOWING ABDOMINAL DISEASES—*James Norman Coombs, M.D., F.A.C.S.* 404
ABSTRACTS - 408

SECTION VII—SURGERY OF THE LOWER COLON AND THE RECTUM

TREATMENT OF HEMORRHOIDS—*Jerome M. Lynch, M.D., F.A.C.S. and Vincent Hurley, M.D., F.R.C.S. (England)* - 409
PERI-RECTAL STREPTOCOCCAL CELLULITIS—REPORT OF A CASE—*Herbert T. Hayes, M.D., F.A.C.S.* - 413
ABSTRACTS - 414

SECTION VIII—EDITORIAL

THE AFFILIATION OF THE JOURNAL WITH THE AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION - 415
THE JOURNAL, ITS READERS AND THE AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION - 415

SECTION X—AFTER "HOURS"

ASTROLOGICAL PHYSICK—*Clement L. Martin, M.D.* - 417
CORRESPONDENCE - 419

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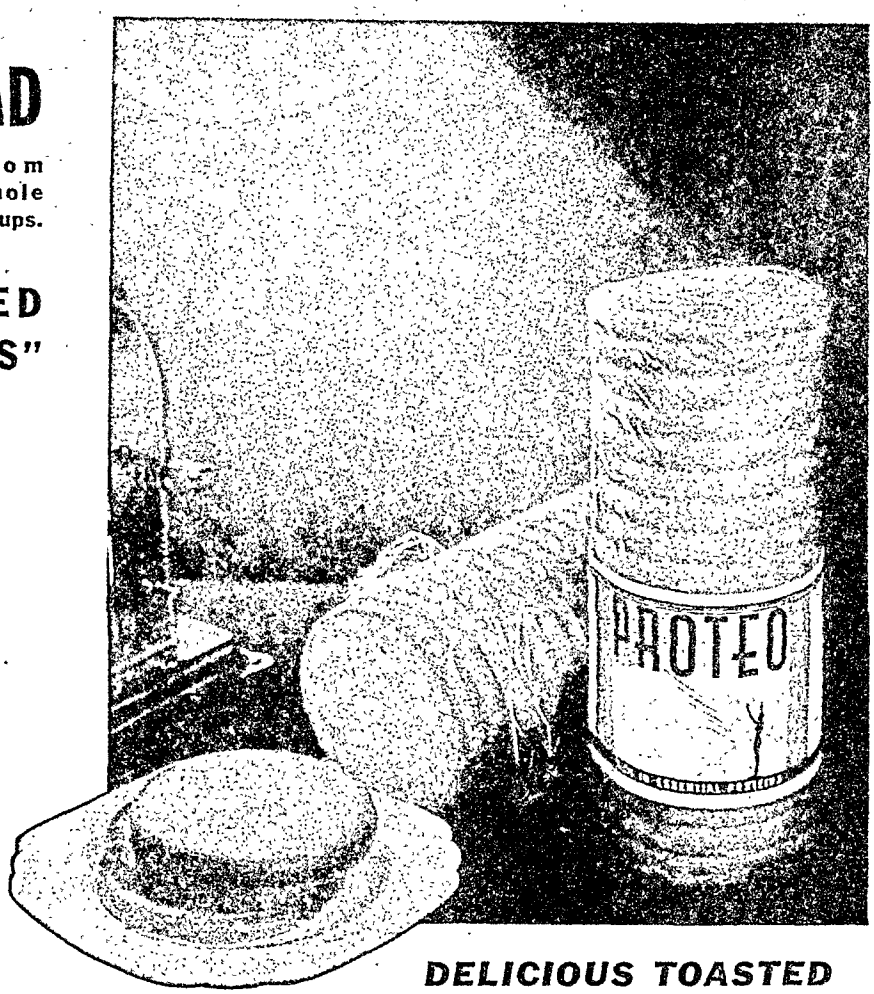
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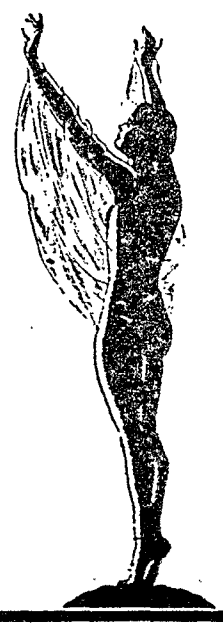
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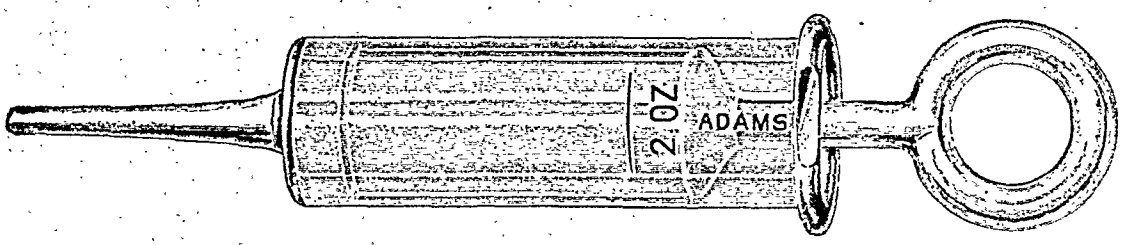
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By M. A. Arafa, M.R.C.P., Medical Assistant, Guy's Hospital, London, with a Foreword by Arthur F. Hurst, M.D., Senior Physician, Guy's Hospital. Octavo, 392 pages, 79 illustrations, including 32 plates, 8 colored, $8.25 (1933).

This up-to-date summary should prove a great value to all physicians and surgeons interested in gastro-intestinal, hepatic and pancreatic disease.

The following review appeared in Surgery, Gynecology and Obstetrics, April, 1934:

"From the observations and experience gathered together from many authorities upon the subject of gastro-enterology, Arafa presents what he considers the modern methods of investigating and treating problems involved.

"In the first two chapters the author gives detailed methods of accurate history taking, physical examination, and radiological technique both of a normal and a pathological stomach; also he shows the value of gastric analysis and the various means and methods of examining the gastric contents. The instruments used and their value in securing a more direct view of the stomach are discussed.

"Chapters III and IV deal with chronic gastritis and peptic ulcer. Various methods of making a differential diagnosis of these conditions are discussed in full and methods of treatment are suggested, including the general principles of the diet that should be correlated with the medical treatment.

"The subject of intestinal disease is opened with a discussion of the clinical physiology of the intestinal tract and its relation to the stomach and its functions. The same general plan of presenting what the author considers the most valuable methods of diagnosis and treatment is carried out.

"In Chapter VIII is discussed cholecystography and duodenal intubation. The technique and interpretation of the results are given special consideration. Dr. Knott has also given a discussion on the method of examining the contents of the duodenum.

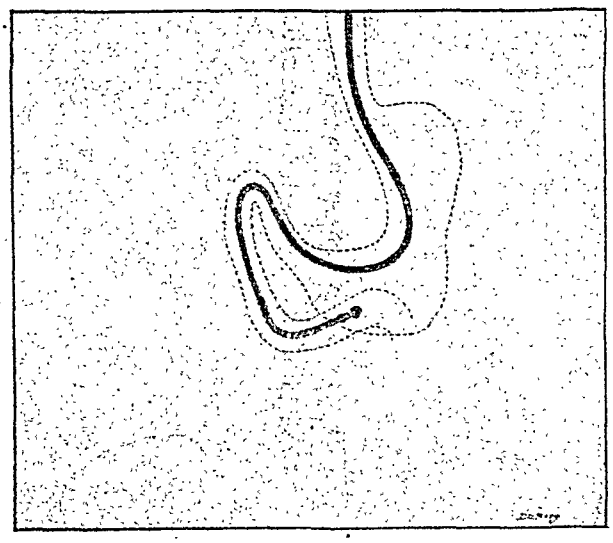
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SECTION I—*Clinical Medicine: Diseases of Digestion*

COMMENSAL AND PARASITIC ENTAMEBA HISTOLYTICA INFESTATION

PARASITOGENESIS OF ENTAMEBA HISTOLYTICA

By

LLOYD ARNOLD, M.D.*

CHICAGO, ILLINOIS

THE epidemic of amebic dysentery in Chicago during 1933-34 has emphasized the importance of this disease in the north temperate zone. Although it has long been known that this disease was not restricted to the tropical and semi-tropical regions, it still was not regarded as a common ailment in the cooler climatic regions.

Several workers in this laboratory have been interested in the bacterial flora of the gastro-intestinal tract and the environmental factors that influenced this bacterial population both qualitatively and quantitatively. The adaptation of the host of enteric bacterial flora may throw some light on a similar mechanism regarding parasitic infestation. The contributions to the subject of the gastric and enteric bacterial flora made by workers in this laboratory have been reviewed (Arnold (1) and (2)). The epithelium lining of the gastro-intestinal tract is as much a body surface covering as is the skin. The contents of this tract are outside of the body and the bacterial flora residing on this body surface varies from a sparsely populated gastric and duodenal to a densely populated caecal and colon flora. The lumen of this tube is continuous, hence some biological controlling factor must play a role in the distribution of this endogenous bacterial flora.

There is a relationship between the acid-base balance and the bacterial flora of the gastro-intestinal tract. Figure 1 illustrates this in the normal, post-digestive tract. The hydrogen-ion concentration of the material within the lumen of the various segments of the intestinal tract is not of itself the determining factor in the regulation of the endogenous flora, but indicates a normal secretory and a properly adjusted physiological digestive apparatus. The mucosa of the stomach, duodenum and jejunum possess the power of regulating the bacterial population residing on its surface so long as these levels of the tract are normal. The bacterial flora and the acid-base equilibrium of the contents of the upper half of the gastro-intestinal tract are as good criteria as are basal metabolism, blood counts, blood chemistry and other demonstrable means of establishing a normal individual. The contents of this part of the digestive tract changes with age (Arnold (2) and (3)).

A decrease in the physiological function of the gastro-intestinal apparatus, due to alteration in nutritional or meteorological environment changes the distribution of bacterial flora in such a way that the lower intestinal type ascend upwards in the lumen of the tract. The extension cephalad depends upon the degree or extent of the maladjustment. In instances of water-borne diarrhea, "food-poisoning," or ingestion of other similar irritants, the coli-aerogenes flora may even extend into the gastric lumen. The acid-base equilibrium is changed toward a neutral reaction and ingested bacteria survive and pass through the tract in a viable state. The splanchnic body surface loses its power to control the bacterial life residing in contact with it when the functional status is disturbed to this extent.

The relative distribution of the bacterial flora within the lumen of the gastro-intestinal tract under varying abnormal states of this tract is shown schematically in Figure 2. The normal illustrates a free acid within the gastric lumen, slightly acid reaction in the upper part of the small intestine. This corresponds to the more detailed scheme represented in Figure 1. The hypo-functioning state in the middle sketch of Figure 2 illustrates a lack of gastric response to the normal stimulus of a meal. An acid deficit is present in the stomach and this is always accompanied by an ascension of the fecal flora upwards. This degree or extent of this cephalad extension varies in the same individual and even more so in different individuals. The bacterial flora within the lumen of the small intestinal tract is not fixed, but moves up and down, depending upon the functional status of the tract as a whole. The last drawing in Figure 2 illustrates the achlorhydric reaction accompanying an acute intestinal upset. The irritating substance or substances may be in polluted water (Arnold and Hull (4)), in protein foods due to by-products of bacterial growth (Arnold and Singer (5); Arnold and Hull (6)) or some extra-splanchnic systemic febrile reaction (Arnold (1)). This schematically represents a gastro-intestinal tract that has lost the power of controlling the bacterial life within its lumen. Bacteria fed by mouth appear in heavy concentrations in the feces; there is little difference in this tract between the bacterial flora of the stomach, duodenum and colon (Arnold (1)).

There have been numerous reviews of the literature on amebiasis. Salmonsen (7) has recently compiled a complete list of these publications. A few recent publications are worthy of special mention in connection with our conception of the epidemiology of certain enteric infections, including clinical amebiasis.

Most authorities emphasize the importance of the

*Department of Bacteriology and Preventive Medicine, University of Illinois, College of Medicine and Research Laboratories of the State Department of Public Health, Chicago.

Submitted July 19, 1934.

equilibrium between host and parasite in discussing clinical, subclinical and carrier states of amebiasis. But some do not recognize the existence of a carrier state. Craig (8) thinks "it is very doubtful if the term 'carrier' should be used at all with reference to infection with this parasite (*Entameba histolytica*), if by it we mean an individual in whom the organism is living as a commensal without the production of lesions or symptoms due to its presence." Dobell and O'Connor (9), Acton and Knowles (10), and Boyers, Kofoid and Swezey (11) hold views similar to those of Craig. James (12) "believes that, normally, the parasites have exacerbations of clinical amebiasis. He considers this a "commensal equilibrium" between parasite and host and not an immunity. He discusses further the influence of hot weather on the increased incidence of clinical amebiasis and considers:

1) Change in the lumen of the colon which alters the food supply for amebae.
2) Increased peristalsis.
3) Change in mucosa of colon leading to an altering of the secretions and weakening epithelial defense.

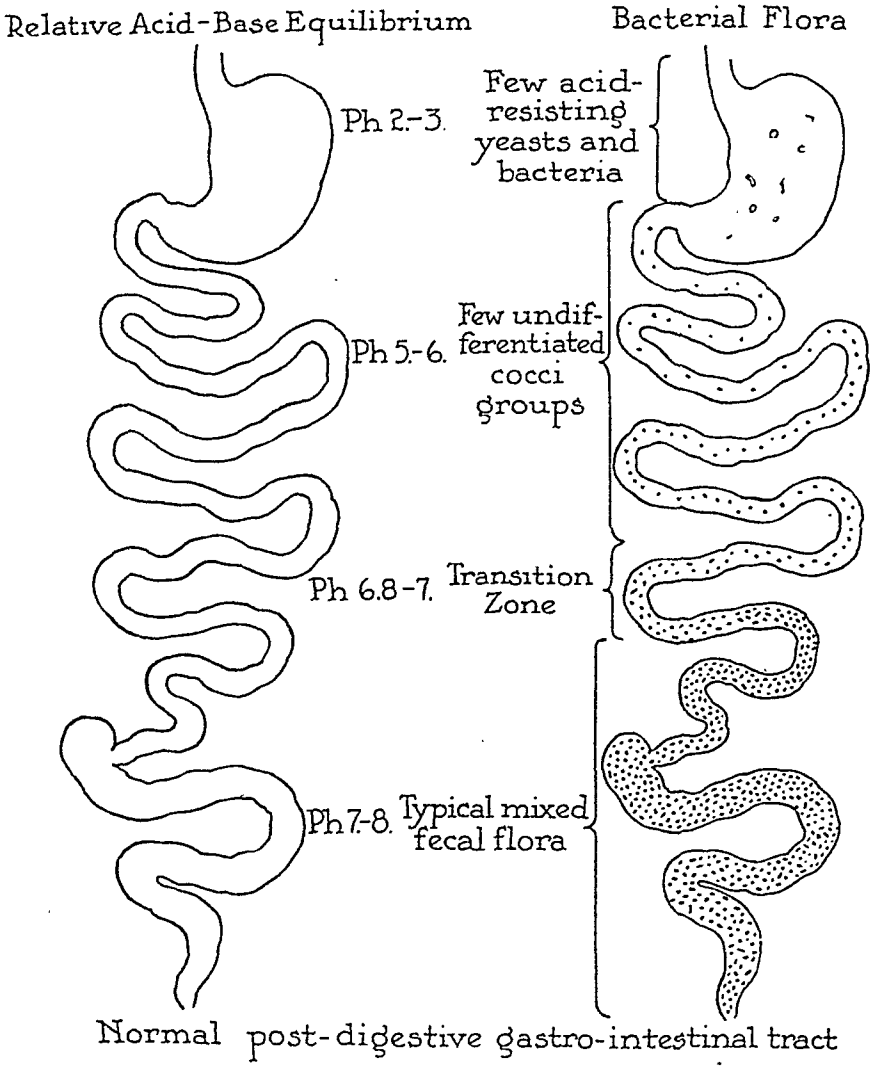


Fig. 1

(E. histolyticæ) live in the lumen of the upper portion of the large gut and that tissue invasion is the part of the few, not of the many." Kessel (13) thinks the amebae can live in the lumen of the intestine merely as commensals and invade the tissues when the balance between host and parasite has been disturbed.

Brug (14) discusses the increase in amebiasis in the summer months in temperate and semi-tropical climates and regards this a change in host and not in the parasite.

Snijders (15) and (16) calls attention to cases of amebiasis returning to Holland from the tropics and without treatment the symptoms subside, but they remain cyst carriers. During hot weather these cases

Dobell (17) infected monkeys with *Entameba histolytica hominis* by feeding cysts. None of these animals (three in number) had dysenteric symptoms and no lesions were observed at any time, although large numbers of cysts were passed in feces for several months. The parasites were isolated and cultured several times from the feces and were found to be identical with the strains fed. *E. histolytica* can live within the lumen of the intestinal tract of the monkey (*M. sinicus and M. rhesus*) without invading tissue. Faust (18) discusses several types of *Entameba histolytica* infestation. A relatively small percentage of cases are acute amebic colitis, a much higher percentage are chronic cases, with obscure intestinal symp-

toms which are relieved by amebicidal drugs. The largest number consist of individuals without demonstrable clinical symptoms, but who pass encysted forms. Faust considered there are minute lesions in the large bowel being produced by the amebae with tissue-repair taking place equally rapidly. Faust makes an exception of heavily infested individuals in a population with a high incidence of infestation and considers the great majority of these individuals have established a complete equilibrium with the host tissue and in some cases possibly not a tissue parasite at all, but, like this organism in certain species of monkeys, is a commensal, feeding only on starch, bacteria and mucous secretions of the large bowel. Simic (19) has reported that 17% of the Slavic population of Macedonia are carriers of encysted *Entameba histolytica*, but only sporadic cases of amebiasis occur in the same population. He fed 12 strains of ameba isolated from feces of carriers to 42 cats to test virulency. Two animals were infected and 40 were negative. Material from the two infected cats failed to infect other cats when transmission experiments were performed. Simic fed four persons cultures from these infected cats with negative results. He also fed six persons with the original strains, as well as injections into rectum, but no dysentery developed.

Reichenow (20) regards the minute microscopic ulcerations in the mucosa of the colon found at autopsy to be rather common and are in the majority of instances due to agonal and post-mortem changes. He quotes Hammerschmidt as having found *E. histolytica* in such superficial lesions. A symptomless carrier was studied by Reichenow and his students. An average of 34 million cysts were passed in feces per day for a period of five weeks, the largest number eliminated within one day was 153 millions. Reichenow thinks a heavy amebic infestation was necessary to produce so many cysts. If these amebae were tissue-growing forms, some symptoms of dysentery should have been present. Reichenow contends most *E. histolyticæ* are harmless. He considers tissue-growing strains derived from clinical cases are more likely to invade tissue and

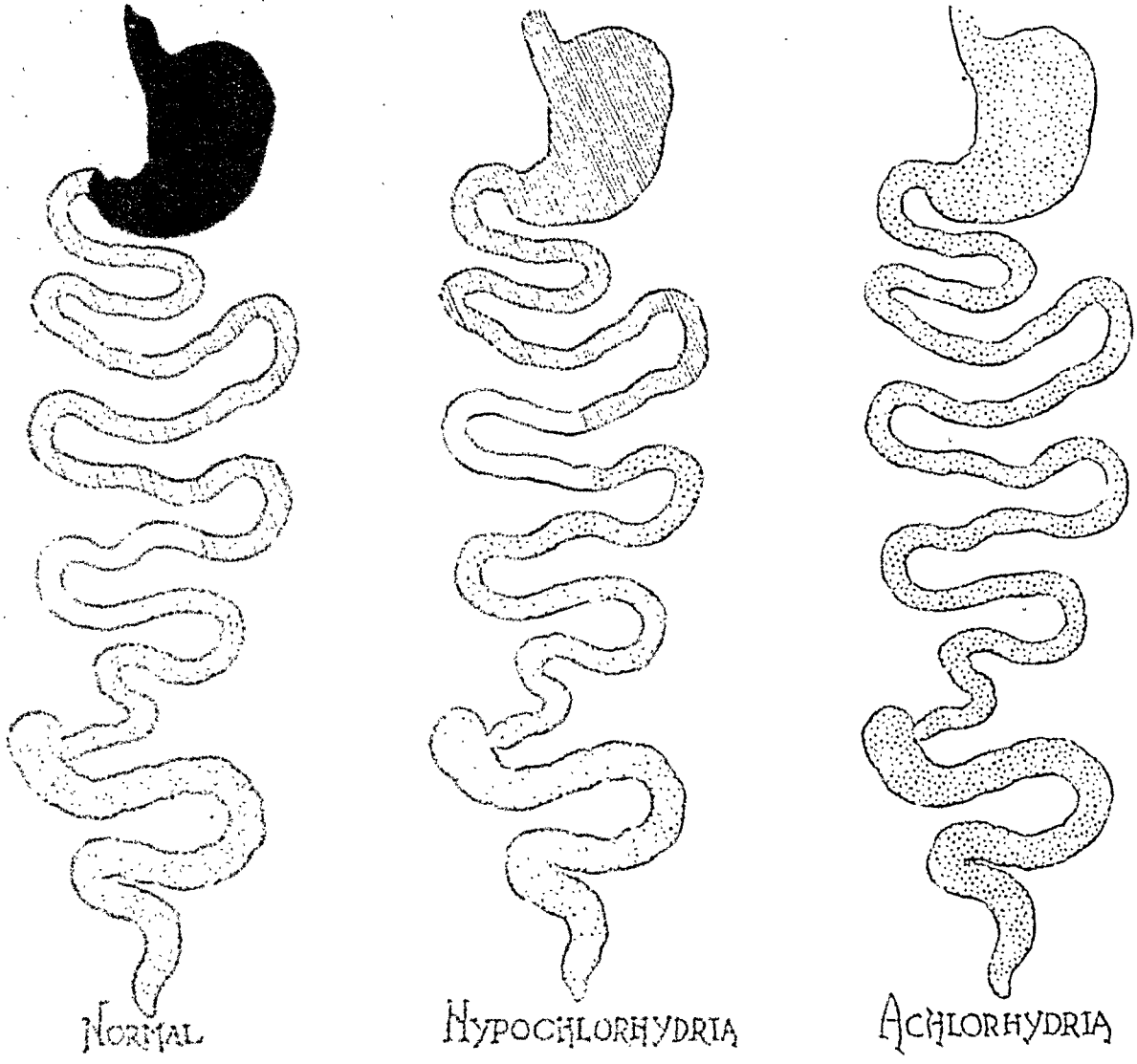


Figure 2.

Normal sketch corresponds to a composite of the two shown in Figure 1.

Hypochlorhydria sketch represents a hypofunctioning gastro-intestinal tract, with diminished gastric acidity and beginning ascension of fecal flora.

Achlorhydria sketch represents a gastro-intestinal tract during acute upset with diarrhea, such as follows water-borne enteritis, "food-poisoning", intoxication and parenteral infections.

are hence more virulent. The colon mucosa can be so changed as a result of hot weather and faulty diet that the lumen-living *E. histolyticæ* will become tissue invaders and symptoms would then follow. The vast majority of the 5% of the population, who carry *E. histolytica* cysts, are carrying lumen-living amebae, according to Reichenow. This author also questions whether the indefinite digestive disturbances, diarrhea and constipation, loss of appetite, lower abdominal pains after meals; or in the absence of these intestinal symptoms, neuritis and various neurasthenic symptoms are really due to amebae. These same symptoms have many times been attributed to other parasites than the ameba. Reichenow (21) brings up the question as to whether these same symptoms encountered in patients without intestinal parasites would not be relieved by the same medication.

Brand (22) counted the cysts of *Entameba histolytica* passed daily by a healthy carrier. The number was so large that Brand could not conceive of them coming from tissue lesions without causing some symptoms. These cysts disappeared within three days under "Yatrin" treatment. Brand considered the enormous number of cysts and the prompt response to treatment pointed toward a commensual intra-intestinal infestation.

Hegner (23) proposes the term "lumen amebae" for the type which lives in the lumen of the intestine. He found no evidence in his monkey amebiasis material to support the assumption that ameba and cysts in the feces are offsprings of the tissue-growing amebae. Amebae are not found passing out of the ulcers in the exudate, but remained at the base and sides of the ulcers. He did not consider it possible for the enormous number of amebae in the lumen to originate from the comparatively few tissue-dwelling amebae. "Furthermore, in carriers where, as most protozoölogists believe, there is no tissue invasion, at least on a large scale, the amebae in the lumen could not be the offspring of amebae in the tissues. The conclusion is that multiplication occurs primarily in the lumen and that only a relatively few lumen-amebae succeed in invading the tissue."

Meleney, Bishop and Leathers (24) found 11.5 per cent of the rural population of Tennessee (20,237 individuals examined) were carriers of *E. histolytica*. The highest incidence (22.8%) was reported from certain isolated hilly regions. Very little evidence could be found of the occurrence of clinical symptoms due to *E. histolytica* infestation.

In a general review of dysentery and its geographical distribution contained in the League of Nations Report (25), the following is quoted from the summary: "The questions as to why amebiasis so frequently causes intestinal and hepatic troubles in the tropics and, on the contrary, remains mostly latent or at least unobtrusive in its effects in the temperate zone, are the most interesting problems awaiting solution at the present as regards the epidemiology of dysentery." "The elucidation of the problem seems to depend on the determination of the efficient causes of dysentery amongst amebae carriers, both in temperate and warm regions; *i. e.*, the causes of the ameba's change from a saprophytic to a parasitic mode of life, or more probably of the cessation of tolerance on the part of the human host."

Acton (26) divides *Entameba histolytica* carriers into three types:

1) *Coprozoic carriers*—those having no lesions and no symptoms.
2) *Pathogenic carriers*—those having small lesions and slight symptoms.
3) *Mixed carriers*—those having both amebae and bacillary dysentery organisms in stool.

Acton mentions two coprozoic carriers, studied by him, with enormous number of cysts in stool. Death was due to pneumonia and autopsy showed no lesions in the intestinal tract.

Faust (27) estimates that five percent of the population in this country living under good sanitary conditions are carriers of *Entameba histolytica*. He estimates the increase in this percentage may go up to as high as 40 percent of any given population living in unsanitated areas. Reichenow (20) claims about the same average infestation of the population of Germany. Craig (8) reviews 27,180 *Entameba histolytica* examinations in this country and shows 11.5% of them were positive for this parasite.

Nedzel (28) working in this laboratory has made some temperature measurements upon the mucosa of the various body surfaces, using a thermophile electrode and a sensitive galvanometer. The experiments were made to determine if there are changes in temperature of the mucosa of the respiratory tract and the digestive tract accompanying or following changes in the temperature of the skin. Dogs were used for our experiments; nembutal anesthetic was administered. The detailed description of the technical procedure and apparatus will be found elsewhere (28). It was found that when the skin of the animal was cooled, this was done by applying an ice cap to a distant skin area, away from the field of observation, the temperature of the respiratory tract (trachea, bronchii and bronchioles) dropped and the temperature of the gastro-intestinal tract was elevated. When the skin of the animal is heated by the application of hot packs, the temperature of the respiratory tract increases and that of the digestive tract decreases. The results of these studies were consistent; there were variations in the ability of each animal to adjust and correlate the temperature of his body surfaces. All followed the same general pattern of reaction. The temperature of the respiratory tract follows that of the skin when the skin temperature is suddenly changed, but this does not last more than a few minutes and then capillary dilation in the mucosa of the respiratory tract takes place and the temperature rises to the control level. The same is true for the gastro-intestinal tract. The skin in the dog differs considerably from that of man. The skin of man possesses eccrine sweat glands and a specialized capillary circulatory system, neither of which is present in the dog. Man uses his skin as a major organ of heat regulation, he uses it as an insulator in winter and a refrigerator in summer. The pelt-bearing animals can only insulate themselves with their skin organ. One would expect much greater variations in the capillary controlling mechanism of the skin and gastro-intestinal tract of man than we recorded for dogs.

The peripheral system (skin, skeletal muscles, respiratory and urinary apparatuses) and the splanchnic system (liver and gastro-intestinal tract) have in general an opposing capillary controlling mechanism. The autonomic or vegetative regulatory machinery keeps those two big vascular beds so adjusted that when there is vaso-dilatation in one, a vaso-constriction occurs in the other. The ability to maintain a physiological equilibrium between these two systems is very important for the health of the individual. Warm weather causes an increase in the skin function and is accompanied by a corresponding decrease in the

function of the alimentary system. The skin becomes an excretory organ; it serves as a refrigerating and cooling apparatus, but to do this requires increased work (sweat secretion) and increased blood supply. The gastro-intestinal tract has the opposite functional status of the skin and peripheral system. We found a change in the distribution of the endogenous bacterial flora in our experimental animals during sojourns in warm and humid rooms. There was an ascension upwards of the large intestinal flora, the contents changed toward a neutral or alkaline reaction. The extent of these changes corresponded to the ability of the animal to adapt himself to the meteorological environment; in some there was a transitory change and in others a period of several hours in which the animal was very uncomfortable. Diarrhea was not uncommon in some of the dogs in hot and humid rooms (Arnold (1)). Assistants carrying on these experiments also varied in their ability to work in these "tropical rooms."

During the warm months of the year, in this climate, we actively use our skin system more than we do during any other season. The cold months of the year we insulate and otherwise protect our skin against heat loss. The splanchnic system has little competition in its vascular requirements during the cool months of the year, but during the warm season our heat regulatory system assumes first place and the digestive system becomes secondary. The opposite orientation occurs during the cold season.

Arnold (1) showed experimentally the relationship between gastric acidification, acid-base equilibrium in the duodenum and intestinal self-disinfection. Diarrhea was produced by feeding sterile bacteriophage lysed *B. dysenterica Shiga* to dogs. Living bacteria fed by mouth during the period of diarrhea could be recovered at all levels of the tract and appeared within a few hours in the feces. Another series of experiments dealt with the gastro-intestinal irritating properties of polluted water. Puppies were used for these experiments. Those in the warm and humid room (fed milk every three hours) were given domestic sewage polluted water to drink (obtained from the Chicago River). These animals had diarrhea; the group fed the same, but given good water, did not have diarrhea. This latter group, though, had an ascension upwards to the middle of the jejunum of their large intestinal flora. There are demonstrable intra-intestinal changes during the period of adaptation to hot weather. The gastric acid secretory response is less efficient, the gastric content is not so completely acidified, and hence the acid-buffered material entering the duodenum becomes alkaline buffered sooner and the acid-base balance shifts toward neutrality or even alkalinity in the upper part of the small intestine instead of retaining its acid buffered radicals until it reaches the ileum. This is accompanied by an ascension of the large intestinal flora up into the hydrolysing and absorbing levels of the duodenum and jejunum. This is the borderline of diarrhea and it required but little further change to initiate increased peristalsis. *This is the non-bacterial or non-specific type of diarrhea.* The gastro-intestinal mucosa is so changed in its function during this time that it has no control over the bacterial population residing within its lumen. We are accumulating evidence which shows dissociation of B. coli takes place during these conditions, but a discussion of this phenomenon would be out of place at this time.

Returning to the subject of this paper, the parasitogenesis of *E. histolytica*, and the relationship between our studies upon gastro-intestinal function and amebiasis. The encysted forms of the parasite are capable of passing through the stomach. Excystation can take place a few hours after ingestion within the lumen of the lower end of the small intestine (Hegner (23)). The trophozoites can produce a cytolytic substance which destroys or changes the covering epithelial cells and aids in tissue invasion (Craig (28)). Hegner describes a mechanical invasion between epithelial cells adjacent to the opening of glands. The *E. histolytica* is the only tissue-invading ameba found in the intestinal tract of man. Encystation can take place in the lumen of the intestinal tract from free living trophozoites (Hegner (23), Dobell (17) and Reichenow (20)).

The change from the commensal or lumen-dwelling to the parasitic or tissue-invading is most likely dependent upon alterations in the function of the host. We know of no instance where bacteria or parasites undergo changes in virulency due to seasonal or nutritional influences. All investigations point toward changes in natural defensive powers of the host. The seasonal incidence of amebiasis is well known. Kligler and Olitzki (29) have studied the seasonal incidence of various diseases in Palestine. They consider that "some physiological disturbance occurs in the intestinal tract which favors more active manifestation of the presence of worm infections and more ready localization of the incitants of bacillary or amebic dysentery." Brug (14) and Snijders (15) and (16) have dealt with the seasonal incidence of amebiasis in great detail; both of these authorities consider the host changes in susceptibility, rather than any alteration in virulency of the parasite, to be the proper explanation.

The encysted amebae can pass through the gastroduodenal barrier, in the normal individual. Few bacteria can do this and hence amebae infestation parallels closer the extent of the encysted amebic reservoir than holds for bacteria. We do not know the intra-intestinal conditions favoring excystation of the ingested cysts. Hatching of cysts and the addition of this parasite to the intestinal flora may require certain environmental conditions, which may explain the varying carrier incidence recorded for various folk. There are no records available showing seasonal variations in cyst carriers. It would be logical to assume from all available information that one could ingest cysts at one time of the year as well as another. The intestinal tract does not possess the same defensive power against these cysts as it does against bacteria. The commensal or lumen-dwelling amebae can be those within the lumen of a healthy, normally functioning intestinal tract. Those conditions which change this tract, hot weather, irritants in food—such as decomposed meat, fish or casein—and polluted water may change the mucosa of the intestine in relation to amebae similar to the way it does to bacteria. Snijders (15) and (16) has discussed just this point at considerable length and places the change in mucosa as of the greatest importance. These conditions may also alter the life cycle of the amebae so as to allow a greater proportion of trophozoites to encysted forms and thereby still further alter the host and parasite equilibrium. Disturbances in the heat-regulatory system, such as fever produced as a result of infection or foreign protein injection, will bring about intra-intestinal changes similar to those discussed above (Arnold (1)). Clinical amebiasis may develop from a healthy cyst carrier as a result of some intercurrent infection disturbing the parasite and host equilibrium by changing the physiological reactions of the intestinal mucosa. Acute exacerbations of quiescent chronic cases can be lighted up in the same way.

The majority of adults do not experience diarrhea when they have some mild febrile reaction. This, however, is common in infants, especially during warm weather, but gastro-intestinal irritation may complicate the upper respiratory disturbances of adults as well as infants during the cold weather season. Clinical amebiasis may develop regardless of whether diarrhea has been a symptom of the parenteral infection.

The development of clinical amebiasis can take place in at least 5% of the population if their amebae can be changed from commensal to parasitic mode of life by some external factor, such as a gastro-intestinal irritation. Faust (27) has very aptly called to our attention that at least 5% of the visitors attending the Century of Progress Fair in Chicago last year were infested with *E. histolytica* before leaving home. Those visitors from unsanitated areas can have up to 40% infestation (Faust). The change from a lumen-living to a tissue-living ameba may well be brought about by altering the host in the manner we have already described. The major factor then becomes the gastro-intestinal irritating factor. Any pollution of the drinking water in a hotel or restaurant would supply this gastro-intestinal irritating substance, causing the usual enteritis. Then clinical amebiasis would develop in the previously infestated group after tissue invasion has taken place. The great variations in the period of incubation of amebiasis recorded by most all authorities may be due to the extent of cessation of tolerance on the part of the host, brought about by the changes due to gastro-intestinal irritation. The summer exacerbations of the quiescent chronic types may be due to a similar mechanism. Reichenow (20) recommends that individuals going to the tropics should have a feces examination for parasites. If *E. histolytica* cysts are present, treatment should be completed before going to the hot climate.

We have emphasized the influence of water-borne diarrhea upon increasing the reservoir of *B. typhosus* (Arnold (1)). The occasional and intermittent fecal *B. typhosus* carrier can be changed to a persistent carrier during periods of diarrhea. There may be something take place in the healthy cyst carrier to cause an increase in the excretion of cystic forms during diarrhea, and thereby expand the reservoir during the period of greatest susceptibility, when a large number of people in the immediate environment is suffering from an acute intestinal upset.

Most public health-minded workers in the north temperate zone have had a thorough training in the epidemiology, control and prevention of communicable enteric fevers. The presence of *B. typhosus* in the feces means a reservoir of a pathogenic bacterium. The tendency is for these workers to place equal weight upon the finding of encysted *E. histolytica* in the stool. The presence of these cysts in the feces of a healthy person examined during a routine survey does not mean that this person has tissue-growing parasites in the large intestine. These forms are most likely "lumen amebae" (Hegner (23), Reichenow (20) and (21) and Dobell (17)).

There is confusion in the minds of health officers in the north temperate zone between the prevention of clinical amebiasis and the prevention of parasitic infestation with *E. histolytica*. Meleney, Bishop and Leathers (24) represent authorities in parasitology, as well as in public health practice, and after finding a parasitic infestation up to as high as 36.8% of the total population, with *E. histolytica*, still "do not believe that treatment of healthy carriers on an extensive scale is indicated at the present time." All individuals found by physicians during the course of their examination to be *E. histolytica* carriers should certainly be treated until free of this parasite. All individuals found to be cyst carriers in routine surveys made by health departments or other agencies should be treated by their family physicians until the infestation has been cleared up. It will readily be admitted that an individual passing cysts is a potential menace, but how can any health department isolate, control, supervise and place restrictions upon at least five people in every one hundred of the general population? It becomes apparent therefore that some practical working method of controlling clinical amebiasis should be given first consideration and leave the control and prevention of infestation until protozoölogists, bacteriologists and physiologists can tell us more about this subject. The Illinois State Department of Public Health termed "latent carriers" the symptomless healthy individuals passing cysts of *Entameba histolytica*. We based this upon the Acton's (26) "coprozoic carriers"; Reichenow's (20) and (21) "healthy cyst carrier" (*zystenlieferant*); Dobell's (17) and Hegner's (23) excellent experiments with monkeys, showing lumen-living amebae with cysts in feces. These workers, as well as Kessel (13), Ratcliffe (30) and others, have shown the monkey has the same type of pathology when the amebae cause dysentery as has the human and that both differ from the pathology produced in kittens. Several recent investigations would lead one to believe that kittens are poor test animals for the tissue invasion properties of *Entameba histolytica hominis*.

The method used to control clinical amebiasis by health authorities must be separated from the methods used to prevent infestation of healthy persons by commensal living intestinal amebae. Reichenow (20) thinks cysts from cases showing clinical symptoms are different from a control standpoint from cysts from symptomless healthy persons with normal formed stool. The dysentery case has *E. histolyticæ* which are tissue invaders and have this property well developed and hence more restrictions should be placed around this reservoir than a healthy carrier.

SUMMARY

The changes in host susceptibility to gastro-intestinal infections have been presented from the viewpoint developed in these laboratories. Definite intra-intestinal alterations have been demonstrated to occur during adaptation of the host to changes of his meteorological and nutritional environments.

The normal mucous membrane of the gastro-intestinal tract possesses the power of controlling the bacterial population upon its surface. The changes in this mucosa, leading to a loss of this anti-bacterial power, are also associated with the development of clinical amebiasis. Commensal, or lumen-dwelling *Entameba histolytica*, may be changed to mucosa-invading and tissue-living forms by decreasing the tolerance of the host. This can be brought about by a variety of gastro-intestinal irritants. The epidemiology of amebiasis must take into consideration and properly evaluate these gastro-intestinal disturbing factors. A healthy, symptomless cyst carrier may be changed to an acute case of amebiasis without the ingestion of exogenous amebae.

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TREATMENT OF PATIENTS WITH FOREIGN BODIES IN THE ESOPHAGUS OR STOMACH*

By

PORTER P. VINSON, M.D.
Division of Medicine, The Mayo Clinic

and

KARL DEISSLER, M.D.
Fellow in Pediatrics, The Mayo Foundation
ROCHESTER, MINNESOTA

ALTHOUGH foreign bodies in the esophagus rarely should be considered as emergency conditions, the earlier they are removed by esophagoscopy, the greater will be the chances of prompt recovery without complications. Direct examination of the esophagus through the esophagoscope is the only method of determining with certainty the presence in this region of foreign bodies which are not opaque to roentgen rays. It is hardly necessary to state that in removing such foreign bodies esophagoscopy is the only method that is worthy of serious consideration. In contrast to this, however, is a great number of cases in which foreign bodies have passed spontaneously through the esophagus into the stomach, or else have been pushed into the stomach at the time esophagoscopy was performed, wherein expectant treatment is indicated.

In cases in which patients have hair balls or other forms of bezoars in the stomach, one cannot expect to remove the foreign body without performing gastrotomy, and this form of treatment frequently is necessary to remove multiple foreign bodies from the stomachs of insane persons. It is remarkable what a variety of foreign bodies may be swallowed by the insane and by performers in side-shows and yet pass through the intestinal tract without producing any symptoms.

In recent months, several reports have been published describing laparotomy and methods for closing an open safety-pin in the stomach, and also for removal of slender types of foreign bodies without the necessity for gastrotomy. Although operations of this type may be very useful in certain rare instances, it should be emphasized that such operations should be delayed for an indefinite period of time in the hope that the foreign body will be expelled spontaneously. Laxatives should not be given, and the patients should



Fig. 1 (case 2). Key in stomach.

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have regular feedings of bulky types of food. If the foreign body is not expelled from the stomach in a reasonable period of time, esophagoscopy and gastroscopy should be carried out under fluoroscopic guidance before laparotomy is undertaken, as this examination can be made without very much discomfort or risk and the foreign body removed through the mouth. It is impossible to set any arbitrary time limit in which a foreign body may be permitted to remain in the stomach without an attempt being made to remove it, but that one is justified in waiting for a considerable period of time is illustrated by the cases, abstracts of which we are reporting. In case 1, the foreign body failed to pass through the intestinal tract after expectant treatment.

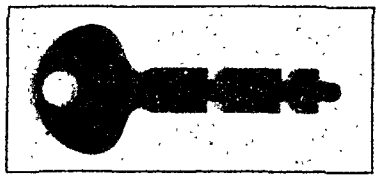


Fig. 2 (case 2). Key after spontaneous expulsion from bowel.

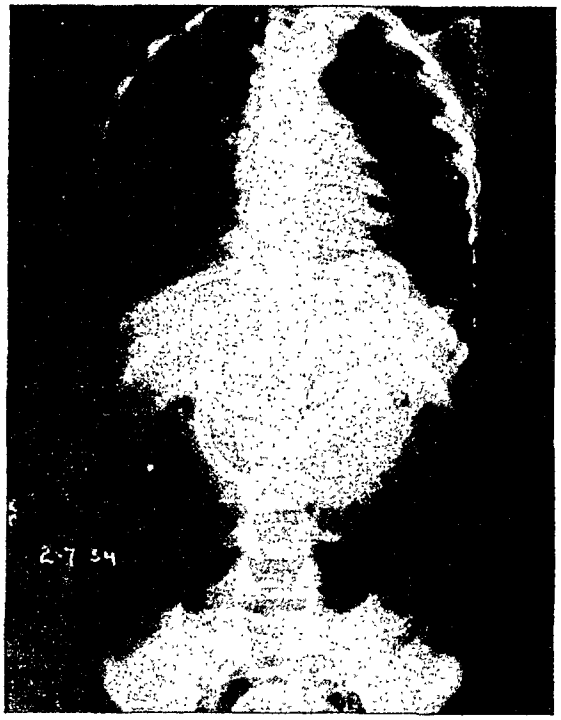


Fig. 3 (case 3). Catheter in stomach.

REPORT OF CASES

Case 1. A man was examined several years ago and was found to have a chronic, perforating, duodenal ulcer. Operation was advised, but the patient demurred. A few months later, he accidentally swallowed a piece of wire. A roentgenogram revealed the presence of the foreign body in the duodenum, and it remained in this position for about a week. Because of the symptoms referable to the duodenal ulcer and also because of the foreign body being in the duodenum, operation was carried out and it was found that the wire had entered the crater of the perforating ulcer.

Case 2. A child, two years and eight months of age, had swallowed a padlock key ten days before coming to this clinic. Operation for removal of the foreign body had been advised because it was thought that the key would not pass through the pylorus. After ten days' observation, the key was passed by bowel (Figs. 1 and 2).

Case 3. A child, three years of age, three weeks before admission to this clinic, had swallowed some type of antiseptic tablet, and gastric lavage had been carried out elsewhere by means of a small catheter. The catheter had slipped from the hand of the physician and had passed into the stomach (Fig. 3). Various opinions had been given as to the type of treatment that should be employed and it had been thought that operation would be necessary to remove the foreign body. However, on expectant treatment at this clinic, the catheter was passed six weeks after it had entered the stomach.

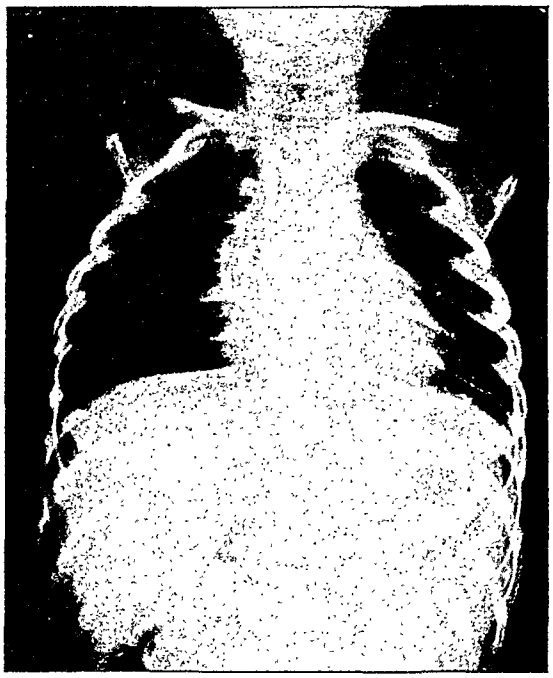


Fig. 4 (case 4). Open safety pin in the esophagus.

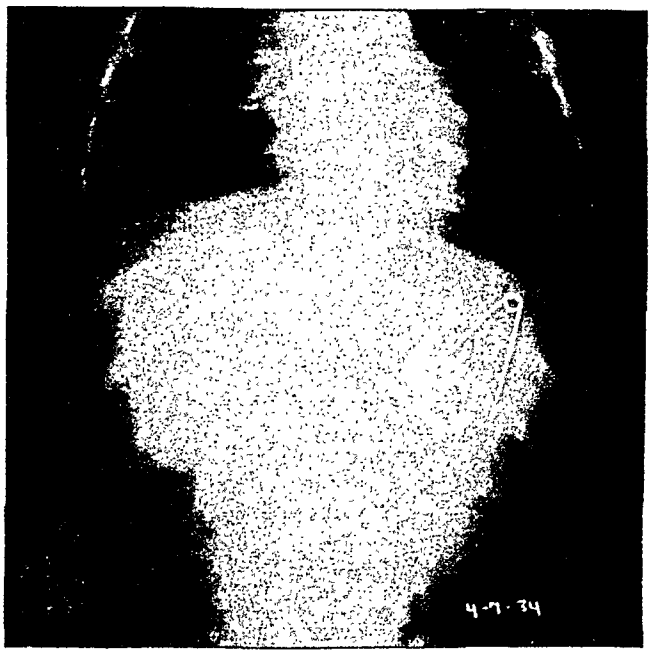


Fig. 5 (case 4). Safety pin after it had been pushed into the stomach.

Case 4. A child, one year of age, had swallowed an open safety-pin earlier in the day on which he was examined at this clinic (Fig. 4). On admission, he had a temperature of 102 degrees F. and grunting respirations. It was feared that the pin had perforated the esophagus. At the time of esopha-

goscopy, the point of the pin could not readily be identified, and, therefore, the pin was pushed into the stomach (Fig. 5). There it remained for two weeks without producing symptoms and, at the end of that time, it was expelled spontaneously.

Not all foreign bodies that have entered the stomach necessarily pass into the bowel; this is illustrated in case 5.

Case 5. A child, eleven months of age, had swallowed an open safety-pin and was brought to this clinic the same day. Esophagoscopy, with the child under general anesthesia, revealed the pin to be in the lower portion of the esophagus (Fig. 6). On passage of the esophagoscope, some embarrassment of respiration occurred, and it was thought best to push the pin into the stomach. Another roentgenogram was made immediately following esophagoscopy and it revealed that the pin had been regurgitated into the upper portion of the esophagus, in reverse position to that which it had occupied before (Fig. 7). Esophagoscopy was again performed and the pin removed without difficulty.



Fig. 6 (case 5). Open safety pin in the lower portion of the esophagus.

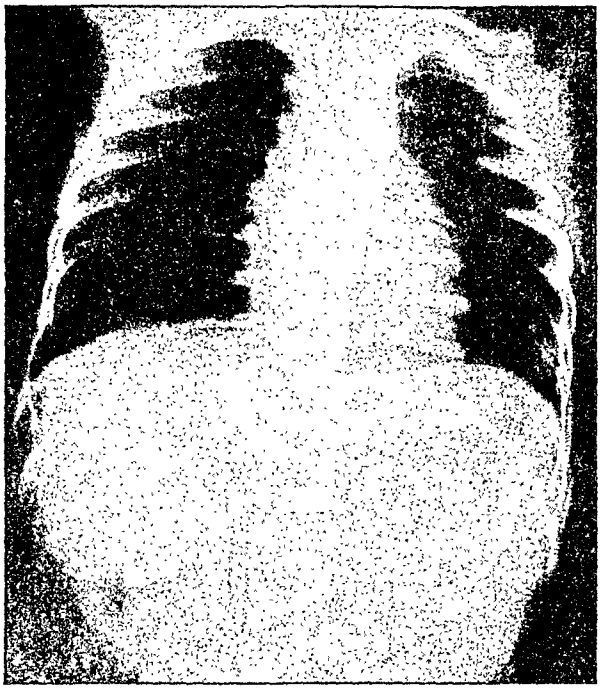


Fig. 7 (case 5). Safety pin after having been pushed into the stomach and regurgitated into the upper portion of the esophagus.

A NEW ASPECT OF MIGRAINE AND CERTAIN RELATED CONDITIONS

WITH A DISCUSSION OF ITS THERAPEUTIC POSSIBILITIES

By

EUGENE FÖLDES, M.D.

NEW YORK CITY, NEW YORK

IN THIS paper, which is the outcome of theoretical considerations and practical observations, in part published in a previous work and in part subsequently arrived at, it is not my purpose to give a detailed description of the symptomatology of migraine. It will be sufficient to say that migraine occurring in otherwise healthy individuals, consists of periodically recurring paroxysms of headache, usually in the form of hemicrania, which are associated with nausea and frequently with vomiting. Visual disturbances and various nervous and psychic manifestations are not uncommon occurrences in these attacks which seriously interfere with the general sensation of well-being.

Aside from migraine, however, paroxysms of headache, vomiting and visual disturbances also are seen in other conditions, among which I will mention uremia and, in particular, that form of uremia which has been variously termed the acute, convulsive, or elamptic uremia. This occurs in such forms of glomerulonephritis, or nephrosis, as are associated with visible retention of liquids; in other words, convulsive uremia occurs in the edematous forms of kidney disease. The most characteristic symptoms of convulsive uremia are the well known tonic and clonic convulsions. These, however, are mostly preceded by violent headaches, vomiting and visual disturbances. Not only are uremic convulsions preceded by headaches, vomiting, and visual disturbances, but this characteristic triad may be the sole manifestation of uremia without the development of convulsions ("uremic equivalent"). Apparently, therefore, the headaches, vomiting and visual disturbances which regularly precede uremic convulsions, or manifest themselves instead of the latter, are caused by the same factors to which the convulsions are also due.

As to the pathogenesis of "convulsive uremia," there seems little doubt that it is the increased intracranial pressure caused by accumulation of fluids in the brain tissue and within the cavities of the brain which leads to convulsions and to the aforementioned triad of headaches, vomiting and visual disturbances. I have mentioned that the latter symptom-complex is the most

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characteristic finding in migraine. The question therefore arises whether the similarity is merely casual, or is due to the working of the same factors in both instances. Having pointed out that, in uremia, the headaches, etc., seem to be caused by such intracranial accumulation of liquids as is part of a general retention, our question can be formulated in another manner, *i. e.*, whether migraine, as well as uremia, is caused by intracranial accumulation of liquids, and whether this, in turn, is produced by general retention.

On first thought, this question would hardly be answered in the affirmative. The argument probably would present itself that it is comprehensible that intracranial accumulation of liquids should occur in glomerular nephritis or nephrosis, in which there is visible retention of liquids in the form of edema, the retention being due to insufficient kidney function. What justification is there, however, in assuming the presence of general retention and of local accumulation of liquids in the brain in the absence of edemas in migraine? And how should one explain retention of liquids in migraine in the absence of kidney lesions and in the absence of circulatory disturbances? These questions would seem reasonable since we are not accustomed to assume the presence of retentions of liquid if there are no visible or other physical signs and, moreover, if there are no organic lesions to account for retentions, such as renal, cardiac or certain endocrine pathological changes.

However, to draw the conclusion that in the absence of visible retentions there can be no general or local accumulation of liquid in the organism is not warranted. It is sufficient to recall the fact which has been known for a long time, but was not always realized, that there may be a retention of even so much as several pounds of liquids without there being a visible edema.

Nor is one justified in saying that in the absence of renal, cardiac, or certain endocrine changes, there can be no general or local accumulations of liquids in the organism. To demonstrate this, I shall have to deviate from the specific subject of migraine into the realm of the physiology and pathology of general water metabolism.

PHYSIOLOGY AND PATHOLOGY OF THE GENERAL WATER METABOLISM

Among the physiological and pathological phenomena of the water metabolism, two occurrences need to be discussed. One is the *retention*, and the other the *mobilization* of liquid.

The term "retention" requires no further elucidation. It denotes an increased liquid content of the organism as compared with that content which would appear to be normal. The term "mobilization," however, requires some discussion. When speaking of mobilization of liquid, I mean the occurrence of a suddenly increased influx of liquid from the tissues into the circulation, leading of necessity to temporarily increased circulating blood-volume and, in the case of sufficient function of the organs of circulation, leading to an increased minute-volume output of the heart. Mobilization of liquid may, but does not necessarily, lead to increased elimination of water through the kidneys. It is obvious that if the mobilized water meets with an obstacle in any part of the circulation, in the sense that it is not carried away from that part with the same rapidity with which it is transported there, a local accumulation (congestion) must result in the same way as in the case of a traffic congestion in the streets of a city. In such cases, the mobilized liquid, formerly retained throughout the tissues generally, is not eliminated through the kidneys, but merely shifted to the place of congestion.. The term mobilization is, therefore, not synonymous with increased elimination; it deals with the intermediary *water metabolism*, rather than with the *water balance*. But even though mobilization of liquid is not necessarily followed by increased diuresis, it is obvious that for the development of increased urinary output a preceding mobilization is a *conditio sina qua non*, since, without mobilization, the liquid remains in the tissues as an inert mass, and because the kidneys are incapable of eliminating that which does not reach them.

In the discussion of retention and mobilization of water, it is necessary to enumerate some of the various factors which influence the water metabolism, aside from the well known influences exercised by the kidney, heart and endocrine functions.

Among the little known factors influencing the water metabolism, the *diet* should be mentioned in the first place. It is a well established fact that a considerable increase in the protein metabolism leads, as a rule, to increased water elimination through the kidneys. Conversely, a protein-poor diet may lead to the development of edemas. It seems that the increased diuresis produced by a diet rich in proteins is generally due to two factors, one being connected with the protein metabolism in general, while the other is connected with the metabolism of nucleoproteids. It is known that one of the strongest and most generally effective diuretics is urea. This, on the other hand, is the chief end-product of the protein metabolism, approximately ninety percent of the nitrogen content of the urine being present in the form of urea. Consequently, the assumption seems to be justified that the diuretic effects of a protein-rich diet are partly due to urea formation, particularly as under these circumstances the amount of urea eliminated with the urine in twenty-four hours averages twenty-five to thirty-five grams, a quantity equal to that which is usually effectively employed when administered as a diuretic. Meat, however, and many of the other food substances which are rich in proteins, contain a certain amount of nucleoproteids as well, and great significance must be ascribed to the latter in the water metabolism. The reason for this assertion is that nucleoproteids contain purin substances, a product of which in the intermediary metabolism is xanthin. Xanthin, in turn, has a close chemical relationship to the diuretics of the caffein group, and it is therefore highly probable that the effect of the ingestion of nucleoproteids on the water metabolism, resulting in increased diuresis, is due to the formation and action of substances similar to those of the caffein group.

The effect of a diet rich in carbohydrates on the water metabolism is quite opposite to that of a protein-rich diet, inasmuch as a carbohydrate-rich diet results in water retention. A fat-rich diet similarly leads to water retention.

Considering that effect which variations of the water intake have on the water elimination, it is generally known that in the presence of certain kidney diseases or decompensated heart lesions, increased liquid intake leads to *retention*, rather than to *increased* urinary output. For this season, the principle of restricted liquid intake has been introduced in the therapy of certain diseases of the kidney and the heart. In the absence of the latter, however, and particularly with reference to the "healthy" individual, it is generally assumed that the water introduced is always quantitatively eliminated through the kidneys, lungs, skin, etc. This is an erroneous assumption. Experi-

ments carried out on normal individuals, who were on an average mixed diet, showed that if the liquid intake was considerably increased, an increased thirst developed unexpectedly, which necessitated the drinking of more and more water. And that this thirst was not due to some psychic influence, and that a surprisingly pronounced retention was engendered, was shown by examination of the blood which revealed a very marked increase in the molecular concentration and in the total dry substances. Thus, through increased water intake, a condition was produced not unlike uremia, a retention disturbance *par excellence*. Furthermore, my own experience showed that the body weight may increase in normal individuals by as much as four to six pounds after one day of increased liquid intake, particularly if the individual is on a carbohydrate-rich diet. Obviously, such changes of the body weight can be due to liquid retention only. While this increased liquid intake may lead to water retention in the "healthy" individual, a restriction of the daily fluid intake on a normal mixed diet leads to increased water elimination. If the restriction of the fluid intake is extreme, however, retention of molecules may occur, although the fluid content of the body decreases. The explanation of the cause of a molecular retention on an extremely restricted water intake is that the upper limit of the concentration in which the dissolved substances may be represented in the urine, is limited. For this reason, if there is not enough available water to carry all the molecules destined for elimination in the urine, a part of these is retained in the organism.

If a certain amount of sodium chloride is administered without the intake of additional water, it is wholly, or almost wholly, eliminated, usually with a considerable water diuresis. Occasionally, it also may happen that part of the salt is retained, notwithstanding the increase in the diuresis. A salt-poor diet, on the other hand, is followed by a certain loss of the sodium chloride and water content of the body.

On the simultaneous introduction of large quantities of water and of sodium chloride, a retention of both develops. Similar to this is the diet of the average person, it being comparatively rich in salt, and not restricted in the fluid intake. Therefore, the average diet may increase the content of the body in the so-called "free water" which is easily mobilized. Such a diet may also lead to salt retention in the "healthy" individual.

In this brief survey an attempt has been made to show how water retention may develop under the influences of the diet, if it is poor in proteins and nucleoproteids and rich in carbohydrates, fats, water and salt. These retentions may develop in any individual, even in the "healthy" one.

Next in significance to the diet in the water metabolism are the *functions of the stomach, liver and pancreas*. Without going into details, attention is called to that which has been mentioned in reference to the important part played by the mobilization of liquid in its subsequent elimination. Mobilization, then, is a process not necessarily leading to increased diuresis, but if a diuresis does occur, it is necessarily preceded by mobilization of liquid, since otherwise the liquid remains in the tissues, and the kidneys have no opportunity to eliminate it. The mobilizer of greatest importance is the stomach. This seems to follow if one considers that the diffusion of hydrochloric acid and water into the cavity of the stomach must necessarily lead to a diffusion of liquid from the tissues into the circulation through what can be likened to a suction process. If hydrochloric acid and water leave the blood to enter the gastric cavity, a certain "vacuum" remains behind, which vacuum is filled from the reservoir of the tissues. Furthermore, if hydrochloric acid enters the duodenum from the stomach it stimulates the hepatic and pancreatic secretions which again draw their excreta from the blood, leaving a "vacuum" to be filled by an influx of liquid from the tissues. Consequently, after a meal a process of mobilization of considerable magnitude develops. It is true that subsequently when the intestinal content is reabsorbed, the mobilized liquid is returned to the circulation and may reach the tissues again. Nevertheless, the result is that water and minerals formerly retained in an idle state in the tissues start circulating and may be offered to the kidneys for elimination. Attention is called to the well known phenomenon of the alkaline tide—an elimination of large quantities of urine which follows hydrochloric acid excretion into the stomach. In the case, however, where hydrochloric acid excretion is absent or diminished on account of some process which impairs the mucosa of the stomach, most commonly a gastritis, not only is the hydrochloric acid excretion and the consecutive suction, resulting in the mobilization of liquid, absent, but the pancreatic and hepatic secretions also are diminished, as well as the mobilization which follows these secretions. As a consequence, in gastritis, liquid remains in the tissues without reaching the kidneys and is retained in the organism in a manner similar to, though not identical with, that which is associated with kidney disease.

The *rôle* played by the internal secretions in the water metabolism need not be entered into, since this *rôle* is generally known and appreciated. While almost all endocrine organs influence the water metabolism in one direction or another, two are of particular significance in an understanding of what is to follow. One is the ovary, the increased function of which, for instance, before menstruation, causes retention of liquid. The other is the pituitary, its posterior lobe promoting, and its anterior lobe, perhaps, furthering, elimination of liquid.

Though described, the effect of the respiration on the water metabolism hardly is appreciated. I do not refer to the water eliminated through the lungs by respiration. I do call attention, however, to the mobilization and increased diuresis which follow hyperventilation, a forced deep breathing. During hyperventilation, carbon dioxide leaves the blood in increased quantities, leaving as it were a "vacuum" behind, similar to that following hydrochloric acid excretion and with similar consequences. Indeed, increased diuresis was observed following hyperventilation. Hyperventilation may occur under various nervous and emotional influences. To illustrate this point, reference is made to the deep and frequent respiratory movements occurring under the influence of emotions, of which actors on the stage make ample use. The effect of nervous and emotional influences on the respiration and the effect of the respiration on the diuresis is of particular significance, because here we have the links of a process which form a chain between the nervous system and the *psyche* on the one hand, and the water metabolism on the other.

Two more factors remain and will be mentioned briefly: One is the barometric pressure, the variations of which have been shown by Smith to produce variations in the water content of the body. The other consists of the influence of infectious diseases, most of which lead to the retention of liquid.

An attempt has been made to present a brief survey of such intrinsic and extrinsic influences on the water

metabolism as are hardly or not at all appreciated. I have endeavored to show that retentions may develop, not only under the influence of disturbed kidney, heart, or endocrine functions, but also following various other changes. Thus it can be understood why unexplained retentions have often been encountered in so-called normal individuals.

If one accepts this concept, the principal difficulty in drawing analogies between the triad of headaches, vomiting and visual disturbances in uremia, on the one hand, and migraine, on the other, is removed. It may then be permissible to examine the question, whether the water metabolism is disturbed in migraine and whether it is of a pathogenic significance, similar to that in uremia.

WATER METABOLISM IN MIGRAINE

Abnormal retention of liquid seems to be present in migraine, as would appear from the following:

A patient suffering from migraine was given the identical breakfast for a period of weeks, each breakfast weighing one pound. Consequently, his body weight was one pound heavier after this meal than before. I observed that if the patient emptied his bladder four hours after having breakfasted, and was then weighed, this weight was the same on most days as before breakfast, the loss of one pound being the result of urination, perspiration and water elimination through respiration. Occasionally, however, there were days on which four hours after breakfast the body weight did not return to the figure obtained before breakfast, obviously because of insufficient water elimination, or in other words, because of water retention. On such days attacks of migraine usually developed.

Another patient suffering from migraine reported having observed that while on days when attacks developed she drank more than usual on account of increased thirst, the urine elimination on those days was decreased to a notable extent. When instructed to measure the intake of liquid as well as the urine output during an attack, the patient reported an intake of 1500 c.c. and an output of 500 c.c. in twenty-four hours. Accordingly, one finds a water retention again.

The fact that after the ingestion of large amounts of cake, candy, etc., attacks of migraine frequently develop has already been described, and has also been reported by several of my patients. I pointed out that such intake of carbohydrates is associated with water retention.

It is also known that migraine paroxysms frequently develop following an acute gastritis, a so-called "indigestion." Attention was called to the fact that gastritis is associated with retention of liquid.

It was shown that water or salt given to women before and during menstruation are eliminated more slowly at this period than in the intermenstrual period, and that in such circumstances the body weight increases, due to the retention of liquid. Again the significance of retention in the pathogenesis of attacks seems to be indicated if one recalls that women suffering from migraine have paroxysms with great regularity before and during menstruation.

Grassheim observed a case of oliguria, which he attributed to pituitary disturbances and in which headaches and vomiting occurred during those periods when there was a complete absence of urination. Here again one meets the simultaneous occurrence of water retention and migraine-like paroxysms. Apparently a similar association is indicated by the case reported by Warner. He observed the occurrence of severe headaches in a patient to whom he had administered large amounts of salt and water simultaneously with injections of pituitrin, thus obviously causing retention of liquid.

It has been observed frequently and has been described that, at the end of the migraine attack, a large amount of urine, the so-called *urina spastica,* is eliminated in many cases. This phenomenon apparently is due to the elimination of liquid retained before and during the attack of migraine.

According to the facts which have just been presented, there are numerous indications of water retention in migraine. These disturbances of the water metabolism are not merely coincidental phenomena, they seem to play a significant *rôle* in the pathogenesis of migraine. This assumption would appear to be indicated by the following observations. The succession of events is such that first the water retention develops and the attack only later, as in the case discussed previously. While obviously this *post hoc* does not prove a *propter hoc,* first water retention and later the attack is nevertheless the succession of events that should be found if the attacks of migraine are caused by water retention. In menstruation there is simultaneously a water retention and the development of migraine paroxysms in predisposed women. One could present the contention that the water retention is an insignificant, coincidental occurrence and the migraine paroxysm is caused by some hypothetical so-called toxic substance or by hormonic influences directly. In the event that this contention is correct, elimination of retained liquid should not prevent attacks of migraine, since the hypothetical toxic or hormonic substances would appear in the circulation, even though there is no water retention, as long as the woman menstruates. This is not the case, however, and with a therapy designed to eliminate and prevent water retention, frequently I have been able to prevent paroxysms of migraine during menstruation; thus evidence is produced as to the causative significance of retention. Similarly, in the case of attacks developing after the ingestion of large quantities of carbohydrates, the subsequent retention of liquid (and no other accompanying change as, for instance, a hyperglycemia) is of pathogenic significance. This seems to follow from my observations, according to which attacks occur particularly in those cases where the intake of carbohydrates is associated with copious drinking. Generally speaking, the pathogenic role of retention of liquid, and not of the manner in which the retentions are brought about, is shown by the observation that a treatment directed against the water retention prevents the attacks of migraine irrespective of their origin. This will be discussed later. Here it should be mentioned that while caffein, an almost universal ingredient of so-called "headache powders," has been used for a long time in the treatment of migraine attacks, it is also a powerful diuretic. Its effectiveness can, therefore, be used as another argument for the *rôle* of retention in migraine.

If it is accepted that water retention is present in migraine as well as in uremia, though obviously to a lesser extent in the former, the next question which requires examination is whether, in migraine, similarly as in uremia, the headaches, vomiting and visual disturbances are due to *intracranial accumulation of liquid.* Evidence of accumulation of liquid within the capsules of the brain is adduced from the following observations. Cushing observed that attacks of migraine are associated at times with choked disk. Subtemporal decompression not only resulted in a

considerable measure of relief in most instances, but also afforded opportunity to note that when subsequent headaches occurred in these patients, the increased intracranial tension was shown by a tendency to protrusion at the seat of the defect, which became flat again or even receded with the free interval. Furthermore, the cerebrospinal fluid was found by Sicard, Claude, Mingazzini and others to have an increased pressure during the attacks. Intracranial accumulation of liquid in attacks of migraine, and its significance has already been advocated by Quincke and Strümpell. The following considerations also favor the assumption that such an accumulation takes place in migraine and is the immediate cause of the paroxysms. It is a generally recognized fact that distention of a tissue is followed by pains. Thus, if an organ is surrounded by a capsule and if the volume of that organ is increased suddenly, distention of the capsule and consequently pains follow. The renal colics, in intermittent hydronephrosis caused by the distention of the capsules of the kidney, should be mentioned as an example. The capsular distention is produced in this case by the increased volume of the hydronephrotic kidney. That the brain is no exception to this rule is shown by the presence of severe headaches in brain tumor. In this case, the tumor increases the volume of the brain tissue, thus leading to distention of the meninges. The example of uremia shows that severe headaches may be caused if distention of the meninges is due to accumulation of liquid rather than to a growth of tumor tissue in the brain. Finally, the presence and pathogenic significance of exactly the same occurrence in migraine as in uremia is suggested by the presence of similar, though quantitatively less pronounced, disturbances of the water metabolism and by the fact that processes leading to water retention often *provoke,* while processes leading to elimination of retentions mostly *prevent* or stop attacks of migraine. Assuming that the tissues not only inside but also outside of the skull are involved in the accumulation of liquid and that, for this reason, in migraine attacks the skin of the head is also distended, it can be understood why the placing of a towel around the head, or that pressure exerted by the hands may alleviate pain. Evidently the distention of the skin is thus counteracted.

If it is accepted that there is a water retention in migraine and that this is the direct cause of the attack, the question as to the *origin of the disturbed water metabolism* should be examined. One finds partly intrinsic and partly extrinsic factors here. The sex hormones should be mentioned in the first place. Previously it has been pointed out that the hormone produced by the ovaries promotes retention of liquid. This occurrence offers an explanation for the observation that before and during menstruation, in other words, in the period of increased hormonal discharge, the frequency of migraine attacks is greatest. In an instructive case described by Thomas, the retention reached such a degree in a woman suffering from migraine that the body weight increased by 11 to 14 pounds at the menstrual period, and generalized edema appeared. Decreased urinary output, severe headaches, choked disks, and increased pressure of the spinal fluid were the additional features of this case. Following the menstrual period there was a profuse polyuria (frequently 4 to 5 quarts in a day) with a rapid return to normal weight. Considering that the male sex hormone also promotes water retention, a case such as the one I observed can be understood. This was an instance where a man suffering from very severe migraine complained of excessive sexual irritability, though fifty years old. The *rôle* of gonads in the pathogenesis of migraine is, furthermore, indicated by the well known observation that attacks of migraine commence at puberty and usually cease or become milder after the climacteric. Another endocrine organ which obviously plays a part in the disturbances of the metabolism of water leading to migrain is the posterior lobe of the pituitary gland (*vide supra*).

The development of migraine has often been attributed to *gastro-intestinal disturbances* and it seems that acute or chronic gastritis is one of the significant factors in the pathogenesis. This *rôle* of a gastritis is comprehensible if one recalls that which has been mentioned previously in respect to the water retention which follows gastritis.

At this point it may be of advantage to draw *a picture of the pathogenesis of migraine,* even though it be only rudimentary. Under the influence of *intrinsic factors* such as the gonads, gastric function, etc., or under the influence of *extrinsic factors* such as the diet, water retention develops in an individual. This retained water is distributed over the entire organism and the water content of the brain tissue increases as well. The brain, however, is surrounded by the meninges. Consequently, when the volume of the brain increases through water retention, the meninges become distended; this distention and the increased intracranial pressure would appear to be the immediate cause of the headaches and of the other symptoms. Should this be the sequence of events, however, then one would meet a serious difficulty. This difficulty consists in the observation that attacks of migraine frequently are encountered precisely at the time of increased diuresis. Thus, for instance, administration of thyroid extract is known to lead to elimination of retained liquid, and during the course of thyroid administration, attacks of migraine have frequently been observed in predisposed individuals. However, if migraine may develop while the diuresis is increasing and retained liquid is being eliminated, the validity of the supposition that water retention is the final cause of the attacks justly can be questioned. Consequently, either our assumption must be abandoned or else an explanation be found for the attacks which develop at the time of diminishing retentions. The starting point of our analysis of the pathogenesis of migraine was the striking analogy between the characteristic symptoms of the latter and of uremia. It is reasonable, therefore, to investigate if in the symptomatology of uremia, phenomena similar to the one now discussed are met, in other words, whether attacks of uremia may develop while the diuresis increases and the edema is decreasing. Indeed, such occurrences have frequently been observed. Thus, lethal uremic attacks were observed following administration of urea as a diuretic. I also observed the development of severe but not fatal uremic attacks after good diuresis had set in following the administration of urea in nephritis. What is the explanation of these phenomena? They can be understood from the following considerations. Attention previously has been called to the fact that elimination of retained liquid must necessarily be preceded by its mobilization. During mobilization, liquid leaves the tissues, pours into the blood, becomes circulating and finally may reach the kidneys, whence it is eliminated. It has been pointed out, furthermore, that if somewhere in the organism there is a local disturbance in the circulation in the sense that liquids are transported *to* that place more swiftly than they are carried *away* from it, a conges-

tion may occur, in the same manner as a traffic congestion develops on an avenue if the passage of cars is blocked through some disturbance, while their arrival to this point is unhindered or accelerated. If the disturbance in the circulation is located intracranially, part of the mobilized liquid instead of being eliminated is only shifted from the distant parts of the body to the brain, causes a swelling of the tissues there, hence the uremic attack. Obviously there is a necessary prerequisite in the development of such uremic attacks as occur while the retained liquid is being mobilized and partly eliminated, which is that *there must be a local circulatory disturbance in the brain.* This is evident, since if there were no such disturbance, no intracranial accumulation of liquid would occur or, if the local circulatory disturbance were somewhere else in the body rather than in the brain, the retained liquid would be shifted to that point rather than to the brain. In other words, one must postulate a local predisposition in the brain in order to explain the type of uremic attacks which are under discussion. This type could advantageously be called the "mobilization type" in contradistinction to attacks which develop while the oliguria persists and while the edema is stationary, or increasing, in nephritis. The latter attacks may be referred to as of a "retentional type." In the mobilizational type of uremic attacks, then, a local predisposition is postulated in the brain. The nature of this local predisposition may be an inherited or acquired disturbance in certain parts of the capillary or venous circulation of the brain. In an interesting case described by Volhard, it was obviously the gravitation which produced a local predisposition in the one half of the brain. In this case of nephritis, convulsions of the left side were observed in a girl who continuously lay on her right side.

If due consideration is given to the phenomenon of the mobilizational type of uremic attacks, it is fair to assume that attacks of migraine may occur on the same basis. The mobilized liquid may accumulate *locally* in the brain, may lead to a distention of the meninges and thus to headaches and to the other symptoms. But, similarly as in uremia, it is necessary to postulate a local predisposition in the brain in the mobilizational type of migraine, since otherwise there could be no explanation as to why the accumulation of mobilized liquid takes place in the brain rather than in any other part of the body. In the other, the retentional type of migraine where attacks develop in the presence of oliguria and increasing retention, the assumption of a local predisposition in the brain is not absolutely necessary. In such cases, it would appear that the brain tissue is simply taking part in the retentions occurring everywhere else in the organism and it seems that when the retention reaches a certain degree, so that the volume of the brain increases and its capsules become distended, attacks will develop.

The theory of the pathogenesis of migraine which I have presented here, offers an explanation for all experimental and clinical observations. Thus, it is known that in predisposed individuals, attacks may occur simultaneously with changes in the weather. Changes in the weather, in turn, usually are associated with changes in the barometric pressure, to the *rôle* of which in the water metabolism attention has been called previously. There is retention of liquid in the organism in the case of decreasing barometric pressure and this retention may lead to the development of a retentional type of attack. Or, the return of the barometric pressure to normal, following its drop, may lead to a release of previously retained liquid and consequently to a mobilizational type of migraine. It was furthermore observed that infections, as for instance the so-called common cold, may be associated with attacks in sufferers from migraine. Again, attention is called to the fact mentioned in the discussion of the general water metabolism, that almost all infectious diseases bring about retentions in the organism. A noteworthy, but heretofore unexplained, observation is that following experimentally produced hyperventilation attacks occur with regularity in patients suffering from migraine. I have pointed out that hyperventilation leads to mobilization of liquid. Moreover, Muck, who described the occurrence of attacks after hyperventilation, also observed that the paroxysm could no longer be produced by hyperventilation, if the patient had previously gone through a period of starvation. This phenomenon can be understood considering the well known fact that a period of starvation is one of the most effective means for the elimination of retained water. Obviously, therefore, if, following starvation there is no retained liquid in the organism, the subsequent hyperventilation cannot lead to mobilization and so cannot lead to a fluid accumulation in the brain. At this point, it should be mentioned that nervous and emotional disturbances are known to be instrumental in bringing about attacks of migraine in predisposed individuals. I have pointed out that nervous and emotional irritations may lead to hyperventilation. Such hyperventilation may lead to mobilization of liquid and to attacks in the same manner as described under experimental conditions.

THERAPY OF MIGRAINE

I have presented a theory of the pathogenesis of migraine. If one wishes to apply this theory to the therapy of migraine, it is obvious that the *chief aim should be the prevention of accumulations of liquid in the organism and the elimination of liquid previously accumulated.* It is easily understood that prevention of water retention and elimination of water already accumulated should have a curative effect in the retentional type of migraine, where the accumulation of liquid in the brain is ascribed by me to the participation on the part of the brain in retention occurring throughout the body. In the mobilizational type, which was found to be due to local accumulation of liquid in the brain which was previously retained in other parts of the body and then mobilized, prevention and elimination of retentions should similarly have a curative effect, since in the absence of retention no mobilization can occur.

If a survey is now made of the possible means of preventing and eliminating retentions, or, in other words, of establishing an "antiretentional" treatment of migraine, attention is first drawn to the utilization of diuretics. Empirically, and on the basis of various other theories, diuretics have frequently been used in migraine. I refer particularly to caffein. It can be stated beforehand, however, that diuretics cannot be expected to secure complete relief in the mobilizational type of migraine. Diuretics, if effective, produce mobilization of water, in other words, they produce precisely the occurrence which plays such a significant *rôle* in this condition. Should a diuretic be discovered, the effect of which is stable and continuous, rather than spasmodic, and which, therefore, does not lead to sudden mobilization, it might be of advantage in the therapy. At the present time, however, the mobilizational type of migraine is *a priori* excluded from an attempt at a therapy which uses the administration of diuretics as the sole measure. But there are seemingly unsurmountable difficulties in the way of this

method of treatment in the retentional type of migraine as well. The most serious obstacle in the utilization of diuretics is their unreliability, as there is not one which is effective in all cases, nor at all times in the same case. The toxicity of certain diuretics, such as mercury preparations, and the undesirable by-effects of others, such as that of caffein on sleep or theobromine on digestion, should also be mentioned. These undesirable effects are of so much more import, because the nature of migraine would necessitate an extensive, if not a lifelong, administration. Accordingly, diuretics cannot be utilized as the only means of antiretentional treatment of migraine, although occasionally they may be of assistance.

Different conditions are met with if the attention is turned to a consideration of nutrition as a possible method of an antiretentional therapy of migraine. The expectation that the best method may be to adapt the nutrition to the therapy is justified by the facts which have been enumerated in the survey of the general water metabolism. It has been pointed out that certain factors in the diet have a very effective diuretic and others a definite retentional influence on the organism. These observations provide the main principles of the therapy under discussion. This should consist of a liberal administration of such food substances as have a diuretic action and should include a restriction of those food substances which produce retentions. A theoretical basis for this regime thus presenting itself, the question as to practical feasibility and effectiveness is answered in the affirmative by the favorable results obtained in migraine by this diet that shall shortly be discussed. Well founded, theoretically, feasible and effective in practice, the great advantages of an antiretentional diet are obvious. Its influence upon the water metabolism is continuous, not spasmodic and not mobilizational, in contradistinction to the pharmacological diuretics and can, therefore, be applied with the same favorable results in the mobilizational as in the retentional type of migraine. Also, in contradistinction to certain diuretics, it is naturally non-toxic, and if well chosen, without any improper by-effects. Finally, as the antiretentional treatment must be kept up indefinitely in most instances to secure lasting results in migraine, all possible objections to a lifelong administration of medicaments are avoided.

DISCUSSION OF PRINCIPLES OF DIETOTHERAPY OF MIGRAINE

To repeat: The main principle upon which such a diet should be constructed is that of the utilization of food substances whose action is antiretentional and the restriction of food substances the action of which is retentional. Upon this principle I have built a diet which I call *antiretentional* and which I describe in detail in a work published in 1933.

The most important features of the *antiretentional diet* are the following: it is rich in proteins, aiming at the utilization of their diuretic action. A liberal protein intake is of great importance, because, not only do the other quantitatively significant food elements not share the characteristic diuretic action of the proteins, but a diet rich in carbohydrates and fats is regularly followed by a retention of liquid. The amount of proteins administered is from approximately 1.5 to 1.8 grams per kilogram, ideal weight. As a basis for figuring the ideal weight, Broca's simple formula is used, according to which ideal weight in kilograms is equal to height in cm. minus 100. Thus the ideal weight of a man of the height of 69 inches is obtained in the following manner: 69 inches are equal to approximately 175 cm.; 175 minus 100 is 75. Consequently the ideal weight of this man is 75 kilograms, approximately 165 pounds. The amount of proteins administered is, therefore, from 110 to 135 grams daily. This corresponds to the elimination of 35 to 42 grams of urea daily, a powerful diuretic in such amounts. The proteins administered should consist to a large extent of meats and, particularly in the initial stages of the therapy, of substances rich in nucleoproteids, such as liver, kidney, sweetbread, sardines, etc. In the antiretentional diet special consideration must be given to the nucleoproteids, on account of the diuretic action of one of their constituents, *i. e.*, the purin substances, which are chemically related to the diuretics of the caffein group.

The amount of from 1.5 to 1.8 grams of proteins per kilogram ideal weight daily is comparatively high. This amount is above the minimum requirement and, according to many authors, may be the source of various disturbances, especially if it is administered mainly in the form of proteins of animal origin. While it is true that the minimal amount with which a protein equilibrium may be maintained is much less than the amount suggested as a significant part of the antiretentional diet, attention should be called to the fact that the minimum is not necessarily the optimum, particularly in view of antiretentional aims. But there are quite a few observations which can be quoted and which seem to show that apart from the antiretentional therapy the administration of such quantities of proteins is advantageous rather than otherwise. I make mention of the finding of Lieb, who kept two arctic explorers on a meat-rich diet for an extended period. Not only did he not observe any harmful results but at the end of the experiment the men showed a ruddier appearance and there was a cessation of the loss of hair from which one of them was suffering. Others found accelerated wound healing in a group of rats fed with a diet rich in proteins. As to the general mortality rate, the interesting observation of Lichtenfeldt may be quoted, according to which the more proteins of animal origin there are in the diet, the lower the mortality rate. However, the administration of from 1.5 to 1.8 grams of proteins daily per kilogram ideal weight for an extended period may be harmful and may not prevent retentions of liquid if it is associated with the ingestion of large amounts of food elements promoting retentions, such as carbohydrates, or fats, or both, and if it is associated with the introduction into the organism of large quantities of liquid. In such cases, notwithstanding the diuretic action of proteins, the carbohydrate and fat-rich diet increases the ability of the individual to retain water and the liquid introduced in large amounts offers at the same time the substance to be retained. It should therefore be emphasized that the antiretentional effect of a high protein diet can only be expected if the other rules are adhered to. Distortions of this treatment such as the advocacy of a high protein intake without considering the simultaneous obligatory restrictions, etc., should be emphatically opposed.

Among the restrictions mentioned, one of the most important is that which refers to the carbohydrates. Restriction of the carbohydrates is necessary in the antiretentional diet on account of the retention of liquid which follows the ingestion of carbohydrates in large quantities. I found it advisable to begin treatment with the administration of approximately 2.5 grams carbohydrates per kilogram body weight and later to increase this quantity to approximately 3.5 grams or more in case that such an increase is indi-

cated in order to maintain the body weight and where the individual tolerance, from the point of view of the water metabolism, allows such a procedure. In the individual previously mentioned whose height is 175 cm. and whose ideal weight is therefore 75 kilograms, the carbohydrate content of the antiretentional diet varies between 150 and 260 grams, or slightly more, daily.

A restriction of the intake of fats is also necessary in the dietary therapy of migraine, because, as mentioned previously, the ingestion of fats is followed by a retention of liquid in the same manner as takes place after the ingestion of large amount of carbohydrates. It has been my procedure to fix the amount of fats at from forty to fifty grams daily, irrespective of the body weight. Theoretically, antiretentional results can also be expected from a diet containing more fats, if the carbohydrate intake is restricted below the amount previously stated. But such a procedure would would involve the possible development of acidosis with its undesired effects. Experience also shows that a restriction of fats is generally much more easily accepted and more faithfully followed by patients than a restriction of carbohydrates below the quantity suggested.

In reference to the intake of sodium chloride, on first thought, a severe restriction would seem necessary, in the same way, as is practiced in edematous conditions in order to reduce water retention. Yet, in the antiretentional diet it seemed to be sufficient to instruct the patients to use salt in their food with moderation and to avoid distinctly salty food, such as soups, herring, etc. While the effectiveness of this therapy—without the complete elimination of salt in the diet—was demonstrated by the results obtained, nevertheless certain cases with insufficient improvement made a search for further perfection of the diet necessary. Seeking a solution to this problem, in several cases where patients did not respond with complete satisfaction to the treatment, they were advised to abstain from the use of salt in cooking their meat and vegetables and told to use it in specific amounts on this food after it was prepared. For this purpose 1 to 2 grams of sodium chloride were allowed daily. The patients were not required to eat special bread (prepared without salt) and were occasionally permitted to have cheese which also contains some salt. The results, however, were not uniform. In one case a definite further improvement was noted (Case No. 1), but in another case the condition remained unchanged (Case No. 9). Finally it is noteworthy that the only patient of the 30 observed so far, in whom the headaches remained unimproved by the antiretentional therapy (although the accompanying vomiting, etc., disappeared) was on an unsalted diet previously to and during the antiretentional treatment (Case No. 10). While obviously, further observations are necessary in this direction, it seems at the present time to be advisable to make an attempt with the salt-poorer form of the antiretentional therapy in those cases in which the response to the moderately salt-poor form of the diet is not quite satisfactory.

Since general water retention and local intracranial accumulation of liquid seem to be the immediate cause of headache and of the other symptoms in migraine, an important measure in the antiretentional management is the *restriction of the liquid intake*. Thus, it can not only be expected that such restrictions as are due to the introduction of an excess of liquid may be avoided, but one may also take into account the diuretic action of salt and other minerals. The amount I usually administer varies between one and one and a half liters including the fluid content of fruits. My observations show that the daily intake of liquids should not be less than one liter. I have found that while a daily fluid intake below this level is not acceptable to many patients on account of thirst, it is also less effective as an antiretentional measure and finally that it is harmful as well and therefore absolutely inadvisable. The restriction of the liquid intake below a certain minimum, which seems to be approximately one liter in the diet I have just suggested, is less effective antiretentionally because, in such circumstances, the available liquid may be insufficient to carry and eliminate all the molecules which could be carried and eliminated if more liquids were available. Consequently, a salt and mineral retention may ensue with an accompanying, though inadequate, water retention. Daily intake of less than one liter of liquids including the fluid contents of fruits over a long period is, therefore, absolutely contraindicated. In patients whose individual tolerance for liquid is higher, the quantity can be gradually increased under careful control of the body weight and of the symptoms. In summer, if the outside temperature is high and perspiration excessive, one or two glasses of water may be added to the amount which has been found to correspond to the individual tolerance.

As to the *vitamins*, obviously all of these must be represented in any nutritional system, planned for prolonged usage, in order to avoid the various forms of avitaminosis or hypovitaminosis. Excessive administration of vitamins must also be avoided so as to prevent the harmful effects of hypervitaminosis.

Finally, consideration should be given to the *caloric requirements*. A high calory diet is necessarily either a high carbohydrate or a high fat diet, or both, and consequently leads to liquid retention. The diet lowest in calories, *i. e.*, a starvation diet, is followed by elimination of retained liquid. Accordingly, the diet used in migraine should be a low calory diet, where the minimum which is sufficient for the needs of the organism and which is not accompanied by any untoward results even if given for an indefinitely prolonged period is administered. The antiretentional diet, as suggested in my previous publication, provided between twenty and twenty-eight calories per kilogram, ideal weight, which was, as intended, a low figure. It should be stated, that, contrary to expectations, I observed no undue loss of weight except in rare instances. Subsequent experience showed that the amount of calories administered can safely be augmented in some cases, and should somewhat be increased in other cases, beyond level previously suggested, always remaining, however, below the limit of the tolerance.

Based on the foregoing guiding principles, I have built a *dietary therapy of migraine*. The following is one example of an appropriate diet:

Breakfast

1 glass of orange juice (6 oz.).
30 grams of toast with one pat of sweet butter.
1 cup of coffee, using one of the brands from which the major part of the caffein has been extracted and to which are added one tablespoonful of cream and one teaspoonful of sugar.

Lunch

100 grams of calf's liver, or in the later period of the therapy a similar amount of lean meat or poultry or fish.
Salad, such as lettuce, tomatoes, etc.
30 grams of bread.
150 grams of raw fruit.

Dinner

150 grams of lean meat, poultry or fish.
Salad and vegetables, containing no more than 17 per cent of carbohydrates.
30 grams of bread.
15 grams of cheese.
150 grams of raw fruit.

After several weeks of the treatment it is usually possible to add from 60 to 150 grams of pastry or pie or cake, etc.

For twenty-four hours, from 3 to 4 glasses of water are administered.

In addition to the diet, phenobarbital, one-fourth of a grain four times a day, was administered in such cases as showed symptoms of nervous irritability or insomnia.

RESULTS OF TREATMENT

Thirty cases of migraine and related conditions of headache were treated thus far in this manner, the first fourteen cases of which were described in detail in the previous publication. The subsequently observed cases showed briefly the following:

Case No. 1. Miss A. G., age 29. Bilateral headaches since childhood occurring, after short periods of relative freedom, for days or weeks and reaching occasionally such intensity that the patient is compelled to stop work for months or years. On antiretentional therapy (A.R.T.), consisting of the diet and phenobarbital, which was begun on December 28, 1928, although no complete relief was obtained, there was an improvement in the severity of the complaints to the extent that the patient could resume her work. This condition lasted until January, 1933, when the therapy was discontinued on account of the occurrence of an illness which was diagnosed by a physician as pertussis. A severe relapse followed and the patient again had to give up her position as an office worker. July 15, 1933, A.R.T. was resumed, yet the improvement, though definite, was not satisfactory. August 18, 1933, the same diet was given but with instructions that no salt was to be used in the preparation of the food but that one-quarter of a teaspoonful of salt should be added daily to the cooked meals. This regime was followed by such a marked improvement in the headaches and other accompanying symptoms that the patient resumed her work (observation till February 17, 1934).

Case No. 2. Mrs. E. P., age 30. Mother suffered from headaches. One brother has epilepsy. Patient has dull headaches on both sides of the head, accompanied by nausea, on the average of every other day since childhood. During A.R.T., with which the patient was under observation from October 29, 1931, till June 3, 1932, the headaches and nausea greatly diminished in severity and frequency, periods of several weeks elapsing without complaints. Even the menstrual periods were occasionally free from attacks.

Case No. 3. Mrs. I. S., age 34. For the last twelve years, periods of weeks or months of dull headaches in the back of the head and both temples with blurred vision daily. Particularly, severe headaches during menstruation. Following A.R.T., improvement to the extent that the headaches and visual disturbances completely disappeared. The patient has been under observation from October, 1930, until January, 1934. During this period similar improvement followed the A.R.T. on three repeated occasions. The treatment was not continuous because upon obtaining relief the patient usually discontinued the therapy.

Case No. 4. Mr. J. E., age 28. Father had epilepsy, committed suicide. One brother had convulsions. Patient is suffering from attacks of hemicrania which usually occur two or three times weekly, while for the past two weeks they are continuous, of increased severity and even extending through the night. On A.R.T. (diet and phenobarbital from Dec. 13, 1931, to Jan. 4, 1932) the complaints disappeared completely on the fourth day and did not recur up to the end of the observation.

Case No. 5. Mrs. L. M., age 34. Mother suffering from headaches. Patient has headaches of hemicrania since youth, formerly occurring only with the menstrual period, for the past three weeks, however, of daily occurrence. The attacks commence in the morning and are occasionally associated with nausea. Lately, gaining weight. During the period of observation with A.R.T., from Dec. 14, 1931, till March 12, 1932, the attacks completely disappeared and even during the menstrual periods.

Case No. 6. Mr. M. B., age 37. Since youth, suffering from attacks of headaches, previously every seven to ten days, for the last two years, twice weekly. The attacks begin in the morning and subside in the evening or the next morning and consist of severe hemicrania and vomiting. The paroxysms are associated with several loose bowel movements, while at other times the patient suffers from constipation. Hay-fever from the beginning of June till the middle of July. The patient was under observation with A.R.T. for three weeks from April 28, to May 18, 1932. During this period four attacks occurred but with greatly diminished severity. While previously the patient was compelled to stay in bed on the days when the paroxysms occurred and could take no food, during the period of observation he was able to be about, continue his work and follow the diet. The attacks were also shorter and not accompanied by vomiting.

Case No. 7. Mrs. R. T., age 38. Mother suffering from migraine. Patient has had headaches since childhood, originally once or twice weekly, for the past few months, however, almost daily. The headaches are severe, appear on one side of the head or the other, begin in the morning with visual disturbances and are associated with nausea. Constant dizziness and drowsiness. On A.R.T. (from September 15, 1932, till August 22, 1933), the dizziness and drowsiness disappeared completely. The headaches appeared only during the menstrual period, but even then were less severe and most of the time without visual disturbances and without nausea. At the end of August, 1933, the therapy was discontinued. In a few weeks, the daily headaches, as well as the dizziness reappeared. On September 30, 1933, A.R.T. was resumed with the same results as previously.

Case No. 8. Miss M. F., age 27. Hemicrania with nausea and occasionally with vomiting once or twice weekly since childhood. The attacks are of such severity that patient is compelled to stay in bed. On A.R.T. (from March 21, till May 16, 1933), the headaches became milder, of shorter duration, vomiting was absent, it was not necessary for patient to go to bed and she could continue work, although the frequency of the attacks was the same as before.

Case No. 9. Mrs. S. W., age 40. Mother and two sisters suffering from headaches. Patient has had attacks of severe hemicrania for the past ten years, formerly only at the menstrual period, lately almost weekly. The attacks are associated with vomiting and last from one to three days. On A.R.T. (diet and phenobarbital, from May 20, 1933, till September 18, 1933), up until August the headaches and vomiting disappeared completely. Then, notwithstanding the diet was changed to the salt poorer form, they recurred again but only during the menstrual period and even then without vomiting.

Case No. 10. Mr. A. M., age 53. Attacks of severe hemicrania since childhood, manifesting themselves during the last ten years four to six times monthly, with visual disturbances and vomiting. The attacks are preceded by an elemination of large amounts of light colored urine and are followed by fatigue and backaches for one to two days. Previous therapy, including vegetarian and salt free diets, (the latter observed by the patient until the beginning of the A.R.T.) ineffective. A completely unsalted form of the A.R.T. was employed in this case with the result that, although neither the frequency nor the severity of the paroxysms changed, the vomiting which accompanied the attacks and the fatigue and backache which followed them disappeared entirely (under observation from June 24, 1933, till December 18, 1933).

Case No. 11. Mrs. G. V., age 41. For the past twenty years attacks of hemicrania with nausea in very severe form in connection with the menstrual period, and independently from the latter, with less severity daily for weeks on some occasions. On A.R.T. (diet and phenobarbital) complete relief on repeated occasions (from July 1, till the beginning of September, 1933; from September 23, till November 18, 1933, and from December 16, 1933, till January 6, 1934). Discontinuation of the therapy was followed by relapse in each instance.

Case No. 12. Mrs. E. S., age 26. For the past two months daily headaches at top and back of head associated with nausea. Since the onset of the headaches, poor memory, drowsiness, and blurred vision of the left eye. Eye examination reveals visual changes, probably due to spasms of the retinal arteries (Dr. N. Nelson). On A.R.T. (diet and phenobarbital) the headaches, nausea, drowsiness and visual disturbances almost completely disappeared (from September 29, till October 27, 1933). At the latter date A.R.T. was discontinued and Fowler's solution administered up to November 10, 1933. Thereupon the same symptoms reappeared, in an even more pronounced manner. On discontinuation of the arsenic solution and the re-employment of A.R.T. all symptoms disappeared with no recurrence to date (February 9, 1934).

Case No. 13. Mr. I. K., age 19. For the past six or seven years severe pounding headaches, occasionally with vomiting, formerly once a month, for the last year twice monthly. During the last four months every day, particularly in the morning, drowsiness, lassitude and fatigue. On A.R.T. (from November

1, 1933, till February 8, 1934), the headaches and the other complaints disappeared entirely.

Case No. 14. Mrs. Y. L., age 45. Formerly on the average of once in two months, during the past three months increasing in frequency and during the past two weeks five times, attacks of severe hemicrania with nausea. Sister suffers from migraine. On A.R.T. (consideration being given to the presence of dia- February 16, 1934), the paroxysms did not occur, not even during the menstrual period.

It may be noted that some of these do not represent typical cases of migraine. Encouraged by the observations, that the response to the therapy was similar in typical, as well as atypical cases, a trial was made in cases of headaches definitely of a non-migrainous origin, although apparently due to similar pathogenic factors (Földes, l. c.). The results were as follows:

Case No. 15. Mr. D. W., age 54. No previous history. For the past week severe daily hemicrania with blurred vision, dizziness, thick speech, recurring inability to remember words for a few minutes at a time, generally poor memory. The examinations showed the following. Occasionally for one or two minutes the patient does not respond to questions although he hears and attempts to carry out orders. Neurological examination otherwise negative. Eye grounds normal. Coated tongue. Soft systolic murmur audible all over the heart, dilated aorta. Pulse rate 100, blood pressure 136/80. Liver palpable. Urine: Moderate precipitate of albumin (sulphosalicylic acid reaction), sugar 2.6 per cent, acetone and diacetic acid absent. Microscopically, red and white blood cells, hyaline and granular casts. On A.R.T., (consideration being given to the presence of diabetes), within a few days all complaints disappeared (from August 20, 1930, to March 9, 1931).

Case No. 16. Mr. G. K., age 39. Gaining weight for the past ten years. For the last one and a half years attacks of severe hemicrania with vomiting from two to three times a week. Blurred vision, independent of the attacks. Four months ago rejected by insurance company on account of albuminuria.

The examinations revealed the following: Weight 221 pounds (100 kgs.), pulse rate 80, blood pressure 144/80. No visible edema. Fluoroscopically, moderate hypertrophy of the left ventricle of the heart. Non-protein nitrogen of the blood 65 mg. Urine: Specific gravity up to 1025, trace of albumin, microscopically, no pathological findings. Examination of the eye grounds showed papillary edema. On A.R.T. (from September 6, 1933, to February 11, 1934), the headaches and vomiting did not recur again. The eye examination showed first a marked improvement and finally on February 9, 1934, a disappearance of the papillary edema. The blurred vision disappeared and repeated examinations of the non-protein content of the blood showed the following results: September 22, 1933, 59 mg.; October 13, 1933, 26 mg.; November 24, 1933, 25 mg.; February 11, 1934, 23 mg.

SUMMARY OF RESULTS OF TREATMENT

The results obtained with A.R.T. in the sixteen cases here described and in the fourteen cases previously published can be summed up as follows:

In fourteen cases the symptoms disappeared completely during the period of observation (from three weeks to seven months, average observation three months). Some of the most severe cases belong in this group.

In nine cases the symptoms disappeared almost completely.

In four cases the attacks diminished in frequency, or severity, or both, to a marked extent.

In two cases there was a complete cessation of all symptoms in the first period (three months and one year, respectively) following the therapy, with a subsequent moderate relapse.

In one case neither the severity nor the frequency of the attacks of hemicrania responded to the therapy, but the vomiting and other symptoms ceased entirely.

The improvements followed the A.R.T. with such rapidity and regularity that they are comparable with that obtained with specific forms of therapy. Considering, that of thirty cases, only one was refractory in so far as the headaches are concerned, and that even in this case the vomiting and other accompanying symptoms disappeared, it will perhaps be possible to use the A.R.T. as a so-called therapeutic test in *differential diagnosis.* In one case which resembled migraine in its manifestations, but which did not respond to the therapy, futher investigation disclosed that in fact, nasal polyps were the cause of the headaches.

Upon the interruption or discontinuance of the therapy a relapse was observed within a few weeks in all cases. In many of these cases various forms of treatment previously had been attempted, but antiretentional therapy was the only one characterized by the patients as giving definite relief. All patients reported an improvement in their sense of general well-being. Particularly noteworthy was the improvement of the gastrointestinal disturbances, such as coated tongue, poor appetite, sensation of heaviness in the region of the stomach and adbominal distentions, which frequently accompany migraine.

CONCLUSIONS

(1) It seems that attacks of migraine and headaches of certain types develop in the presence of retention of liquid in the human organism, the brain tissue taking part in this retention (retentional type). Or, these attacks develop if liquid retained throughout the body becomes mobilized, shifted to the brain and accumulates therein (mobilizational type). In both cases the intracranial pressure increases, leading to distention of the meninges: the immediate cause of the headaches and other symptoms of migraine and certain related conditions. (2) A diet, termed as "antiretentional", has been developed, with the aim of (a) eliminating and (b) preventing the retention of liquid. A description is given of the results obtained in thirty cases of migraine and certain related conditions.

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For additional reference see Földes, l.c.

ABSTRACTS

ALVAREZ, F. M., AND FARINAS, P. L.

A Comparative Diagnostic Study of the Biliary Tract and the Cholecystography in the Chronic Non-lithiasic Cholecystitis. Revue des Malad. du Foie (Paris) No. 5, 1933.

These studies were performed partly under the auspices of Prof. G. Parturier and partly in the Clinical Institute of Havana. The general statistics include 202 cases of which 26 only were surgically verified. This is easily explained by the fact that the chronic non-lithiasic cholecystitis does not belong to surgery as does the sclero-atrophic cholecystitis, while on the contrary, the calculous cholecystitis have been automatically handed to surgery. In each of these cases the following examinations were performed: the Graham-Cole test, the Meltzer-Lyon test, the study of the gastric HCl, and the clinical examination.

Their observations were classified in 3 groups: (1) The chronic infectious cholecystitis, divided into 4 varieties; (a) Sclero-atrophic cholecystitis, (b) Simple infectious cholecystitis, (c) Cholecystitis with catarrh of the cystic duct, (d) Cholecystitis due to parasites in the duodenum or biliary tract. (2) Cholecystitis (or the ectasy of the gall bladder). (3) Pericholecystitis.

The authors give the results of their investigation in almost a mathematic way—into these different types of cholecystitis, under the headings of cholecystography, Meltzer-Lyon test, gastric chemistry, and clinical examination. One will then easily understand the immensity of such a work and thank the authors for their arduous endeavor to introduce more clarity in that still obscure field of our medical knowledge.

According to Alvarez, cholecystography (Graham test) is a method of great importance for the diagnosis of the chronic cholecystitis without gall stones in the following circumstances: (a) when the cystic duct and gall bladder are patent, then the dye is more or less concentrated and shows the functional integrity of the gall bladder. Two possibilities only remain in which a true interpretation of the variations of the opacity may be given. (b) When there is found some modification of the localization of the gall bladder, associated with an enlargement of the shadow at its basic part, or when there is marked delay in gall bladder emptying, e. g., cholecystatony. (c) When defects in the bladder contour and emptying difficulty are noted, e. g., in the pericholecystitis.

The Graham test is of minor importance (a) when there is complete "bloquage" of the cystic ducts of the gall bladder, then there is no shadow. Such is the case, as a rule, in the sclero-atrophic cholecystitis. Further, a negative Graham test may be attributed to some obstruction of the biliary tract, to a catarrh of the cystic duct, and, according to certain schools, to a very inconsistent elimination of the dye by the liver.

The Graham test is to be considered of dubious value when the shadow is hazy. The authors believe that too much importance should not be given to the slight differences in the intensity of a shadow, or to the slight modifications in the gall bladder's emptying time. In 90 per cent of the cases of simple infectious cholecystitis without "bloquage" in the cystic duct, with parasites, or in atony of the gall bladder, the Graham test practically is negative, although the functional capacity of the gall bladder is interfered with.

The Meltzer-Lyon test, (1) Has a major diagnostic value in the chronic cholecystitis without gall stones: (a) when the gall bladder response is markedly abnormal or absent or when they show a pathological bile "B". This is the case in most of the sclero-atrophic cholecystitis and in the great majority of the atonic gall bladders. (b) When the examination of slides of biliary samples shows obvious signs of gall bladder infection, cystic catarrh or the presence of parasites. (2) Medical drainage is questionable (a) if the variations of the gall bladder response are too slight and the changes of bile "B" too slight. This will be observed at the onset of certain instances of infectious cholecystitis and in certain cases of atonic gall bladder. (b) If owing to a technical error (possible in a non-specialized laboratory) the macroscopic examination of the bile is in contradiction to the previous findings. (3) The method is worthless (a) when the gall bladder mucosa is not altered, very often when the infection is intramural. (b) In the strawberry gall bladder. (c) In the pericholecystitis.

The clinical examination is of major importance when the gall bladder has lost entirely its functional capacity, e. g., sclero-atrophic cholecystitis, and when the clinical signs have somewhat a specific character, e. g., in the case of "toxo-anaphylactic syndrome" pertaining to the atonic gall bladder. The clinical examination, while insufficient alone for making a diagnosis, should at least give one a general orientation of the nature of the case.

Gastric Chemistry: In the great majority of cases hyperchlorhydria has been shown to be the most frequent factor accompanying the chronic cholecystitis without gall stones, owing to a predominant vagotonic condition, but this is a most variable element in the diagnosis.

In conclusion, the authors believe that the history, along with a Meltzer-Lyon and Graham test should enable one to diagnose diseased gall bladder without gall stones.

Regarding infectious sclero-atrophic cholecystitis, great stress is laid on the viscosity of the bile "B", similar in color to "mint liquor", with the presence in high quantity of flakes and mucus as well as columnar epithelium (Lyon). Also much importance is laid upon the finding of a quick and spontaneous gall bladder response before any duodenal injection, joined to an intermittent leakage of bile "B", and a slower response after the magnesium sulphate injection (Chiray, Lyon, Swalm). Such are considered by the authors as positive signs of infectious cholecystitis. The presence of shaggy mucus or of flakes in an oily substance is, according to the authors, a sign of a cystic catarrah; this is in contradiction with Bockus, who believes that these are due to a mixture in the duodenum of the gastric juice with bile.

Five cases showed parasites: 2 Anguigilus and 3 were cases of Lambliasis. Their origin may have been the biliary tract, as well as the duodenum.

The clinical aspects of the gall bladder ectasy, are given as follows: a sensation of giddiness and attacks of migraine, "urticaire", bilious attacks, all of which are of anaphylactic nature; but in addition will be found gastric manifestations such as burning, pain and cramps of a reflex nature. Constipation and flatulence are also frequent. The article is accompanied by a statistical table for summarization.

Comments: Objections may be raised by those critics who grant little importance to the diagnosis of an infectious cholecystitis, demonstrated by septic bile, as obtained by drainage—the post-operative specimen showing too often a different microscopic flora. Others may object to a diagnosis of non-lithiasic cholecystitis, in the absence of post-mortem or surgery. Many will explain the inconsistency of the authors' results by the systematic use of unphysiological methods. Most of us, however, will admit the sincerity of this extensive study, undertaken with the object of determining the relative value of our actual clinical methods of investigation. Others might suggest newer and more reliable methods of study.

Jean R. A. Le Sage.
(Montreal)

WEINBREN, M.

Right-Sided Duodenum Inversum. Lancet, 226, Feb. 10, 1934, 280-84.

Sandera has reported 10 cases in the last year and the author has found 11 more cases in his own practice in the same period. Sandera considers right-sided duodenum *inversum* to belong to the congenital abnormality known as mobile duodenum. The latter he defines as a congenital dystopy due to faulty or defective attachment of the duodenal mesentery; in association with it may be found abnormalities of the pancreas, right kidney, portal vein and transverse mesocolon.

The normal duodenum as described in the textbooks is divided into four parts, viz., superior, descending, horizontal and ascending. In right-sided duodenum *inversum*, at the inferior flexure, the third part, instead of going to the left of the second part, turns up to the right of the second part and goes on to form the duodenojejunal junction which likewise may be abnormally situated. It may or may not give rise to symptoms, but it is considered that the abnormal passage hinders the normal outflow of the parcreatic and biliary secretions, thus tending to lead to disease in either of these organs. There is no general delay in the emptying of the stomach. When symptoms do occur they resemble those of a duodenal ulcer and are referable to the stomach. There is frequently a diarrhoea which Sandera attributes to a pancreatitis.

Eleven cases are described. They varied from 26 to 70 years in age. Their symptoms are always present for a number of years. The condition can only be diagnosed by X-ray with the patient in the vertical position. It is thought to be due to a congenital error in development.

J. J. Day.

HAFT, HENRY H., M. D.

The Colon Changes in Chronic Arthritis Compared with other Chronic Diseases. Am. Jour. Med. Sc., June, 1933, p. 811.

A clinical study of 25 chronic arthritis cases and a similar study of 25 dispensary patients with non-arthritic chronic ailments revealed a high incidence of ileocecal valve incompetencies, reduplications, lack of haustral markings and atonies. A larger percentage of ileocecal valve incompetency was observed in the arthritics than in the controls, the significance of which the author does not attempt to explain. He suggests that "the expression of the abnormalities in the bowel of the arthritics, as well as in the control cases, is manifestation of chronic diseased states rather than a condition which is peculiar to the chronic arthritides". Allen Jones.

BURNETT, FRANCIS LOWELL, M. D., AND OBER, FRANK ROBERTS, M. D.

Arthritis, Anabolic Nutrition and Health. A study of the Nourishment and Health of Joints. Am. Jour. Med. Sc.

(From the Health Class for Arthritis at the Peter Brent Brigham Hospital.)

The authors state that "a failure of nutrient substance to construct or preserve normal bone and cartliage, i. e., a metabolic disorder, has been often considered as the cause of arthritis". They quote Minot: "little is known concerning the difficulties of absorption and utilization of food products from the digestive tract and regarding what particular food factors may improve gastro-intestinal function. . . . It is probable that significant degrees of such disturbances may arise in arthritis and be overcome by well chosen diets." The authors feel that the Fletcher and Graham diet by improving colonic function may favor the nourishment of the joints. To favor what is termed "anabolic nutrition", the patients are educated to eat and live in order so to operate the proximal colon that entirely segmented feces and normal intestinal rates are produced." A detailed inquiry into the patients' ways of eating and living is made. Studies revealed that poor fat digestion was most common, starch the next and protein the least. Some stools had an acid reaction which was changed to alkaline by treatment. Erroneous eating and the taking of laxatives caused diarrhoea or soft stools. Fig. 2 shows the entirely segmented or normal human feces with which the normal intestinal rate is correlated. Together these indices signify complete digestion and absorption ("anabolic nutrition").

With the prescribed foods, seeds are given and their first and last appearance in the feces is to be noted by the patient. As an example, a case record showed the first of the seeds in 13 hours and the last in 61 hours. The first figures constitute the initial rate and the last the final rate. These figures signify a rapid intestinal rate according to the authors; they prefer approximately initial rates 38 and final 110 hours, with segmented formed feces.

The authors give details regarding diet which are too extensive and detailed to be included in an abstract. They advise long continued co-operation on the patients' part and feel that gratifying results will follow in a considerable number of patients afflicted with chronic arthritis. Allen Jones.

AITKEN; R. S.

Treatment of Profuse Bleeding from the Stomach and the Duodenum. Lancet, 226, April 21, 1934, 839-42.

This is an analysis of 262 cases of bleeding from the stomach and the duodenum from the point of view of estimating the value of the various forms of treatment used. In 7 cases death was due to other causes. There were 27 deaths in the remaining 255 cases giving a mortality of 11 per cent. Of the 255 cases, 192 were very mild cases, were treated medically and will not be discussed further. The remaining 63 cases were cases of severe hemorrhage. Of these 31 were treated medically. There were 17 deaths and 14 recoveries. Most of the patients died directly from exsanguination. Of this group 5 may be excluded, but the author feels that the remaining group of 12 deaths, comprising about one-third of the grave cases so treated, should not be regarded complacently. Of the 11 cases treated medically, but with the addition of blood transfusion, there were 3 deaths. In the group of 21 cases treated surgically there were 7 deaths. The author feels that from the high mortality among cases of severe hemorrhage treated along conservative medical lines, that this form of treatment is open to criticism. He also thinks, that from these figures surgery in expert hands is not necessarily a sentence of death. He recommends that cases of severe hemorrhage (i. e., those in which the red cells are below 2,000,000) should be confined to bed with sufficient morphia to ensure complete rest. They should be given a transfusion of 500 c.cm. of blood without moving from the bed. If the bleeding persists or there is further hematemesis, the transfusion should be repeated once or twice in the next 24 to 48 hours. If the bleeding continues or the patient's condition fails, operation with the minimum procedure to secure the bleeding point along with another transfusion should be immediately undertaken. J. J. Day.

WRIGHT, HAROLD E., AND FREEMAN, ELMER B.

New method for visualization of the unobstructed esophagus. Radiology, XXII, 160-162, Feb., 1934.

Studying deglutition in persons who had never had the slightest dysphagia nor any history of temporary cardiospasm the following findings were elicited: 1. Barium swallowed at the end of full forced inspiration passed leisurely through the cardia. 2. When respiration is suspended in the midst of normal in- or expiration, swallowed barium passes very rapidly through the esophagus and the cardia in a thin stream. 3. Barium swallowed at the end of full forced expiration is held in the esophagus for several seconds and causes a rather remarkable dilatation of the organ, which, in some cases, is almost as marked as is seen in early cardiospasm. A quantity of more than two or three moderate swallows is apt, by sheer weight and volume, to overcome the temporary sphincteric action, and the whole mass then rushes pricipitately into the stomach.

Satisfactory films in the majority of cases were obtained in the erect right anterior position after having the patient aërate the lungs and then at the end of completely forced expiration swallow two or three mouthfuls of thick barium mixture. The exposures are made immediately. Rehearsal of the expiration and swallowing is an aid to more uniformly successful results.

A brief discussion of the prevailing views upon vago-sympathetic innervation, musculature and function of the lower esophagus emphasizes the meagerness of our present knowledge respecting the lower esophageal structure and function, either in the normal or pathological individual. The authors have convinced themselves that mechanical factors respecting the respiratory changes within the thorax have some effect upon the deglutitory function. They also note that there is an anatomical feature in the course of the lower third, because in long-chested persons a satisfactory shadow of the filled esophagus is usually obtained on the first attempt, whereas individuals of short chest and wide costal angles frequently give considerable difficulty even to not infrequent failure.

A few individuals have been found in whom retention of barium in the esophagus is best achieved at the end of full inspiration. The suggestion is offered that these individuals may be potential cardiospasm cases, in view of the fact that this reversed reaction is characteristic of all the cardiospasm cases which the authors had studied.

James T. Case.

KIRKLIN, B. R.

The value of the meniscus sign in the roentgenologic diagnosis of ulcerating gastric carcinoma. Radiology, XXII, 131-135, Feb., 1934.

The value of "the meniscus sign" in the diagnosis of ulcerating carcinoma, which was first described by Carman in 1921, is reiterated with several illustrative cases in which the roentgen diagnosis was made very early in the disease, in fact so early that the surgeon was reluctant to accept it until the stomach itself was opened.

The sign depends upon the fact that ulceration has taken place upon the top of a small mass which projects into the lumen of the stomach, in contrast with benign ulcer which projects outward from the lumen into the gastric wall. Demonstration is best made with small amounts of barium in the stomach, and palpatory pressure as with the usual mucosal-relief-technique. On the lesser curvature in its vertical portion, the crater is seen as a crescentic shadow with its convexity directed outward, a typical "meniscus". Distal to the *incisura angularis* on the lesser curvature, the base of the crater bends with the wall and the meniscus is concave above. On the posterior wall of the stomach, the crater appears under pressure as a dense irregularly rounded shadow encircled by a transradiant zone which corresponds to the elevated border. Of significance in the production and appearance of the sign, is the slightly raised, overhanging border which under pressure gives the separation of the crater from the surrounding stomach content, and results in a slow emptying when manipulated. The *rugae* adjacent to the ulcer are obliterated also.

In differentiation from benign ulcer, ulcerating gastric carcinoma does not project beyond the lumen of the stomach when seen tangentially as a *niche;* the *rugae* about it are obliterated, not accentuated and convergent as in simple ulcer; occasionally the base of the ulcer has a somewhat irregular profile; a mesially seen crater on the posterior wall usually has an irregular margin; spastic phenomena are notably absent; the lesion is not tender, and occasionally may be palpable. Barium pent up between hypertrophied rugae can easily be dislodged. Benign, indurated, saddle-ulcer on the distal lesser curvature projects beyond the lumen prominently and is convex above, whereas the crater of ulcerating carcinoma does not protrude appreciably, if at all, and its base is concave above.

Findings of the "meniscus" type are considered pathognomonic by the author and are certainly conducive in careful hands to a much earlier recognition of the presence of malignancy in the stomach. James T. Case.

SECTION II—*Experimental Physiology*

A FURTHER PROOF THAT THE GALL BLADDER EVACUATES VIA THE CYSTIC DUCT*

By

W. L. VOEGTLIN, M.D.; H. GREENGARD, M.D.,

and

A. C. IVY, M. D.

CHICAGO, ILLINOIS

THAT the gall bladder in fulfilling its physiological function, evacuates by way of the cystic duct is a concept accepted by the majority of investigators.

Lake (4), Lyon (5) and others have noted a decrease in the size of the cholecystogram following stimulation of the visualized gall bladder and a simultaneous increase in the concentration of iodine in the duodenal contents as drained with the Rehfuss tube in human subjects. In order to determine if these findings were applicable to dogs as well, this work was repeated by us on five dogs with results which agree with those of the forementioned authors (see Table I). Likewise

TABLE I

Showing the decrease in the size of the cholecystogram and coincident increase in iodine in the duodenal drainage after cholecystokinin injection (dog).

		Dog Number				
		1	2	3	4	5
Before Injection	Visualization	Good	Good	Good	Good	None
	Bilirubin mg./100 c.c.		23.5	21.0		4.4
	Iodine mg./c.c.	0.48	Trace	0.77	0 48	0.19
After Injection	Decrease in G-B Shadow	50%	40%	50%	30%	
	Bilirubin mg./100 c.c.		97.3	137.1		82.6
	Iodine mg./c.c.	1.30	3.20	3.33	1.17	0.98

Voegtlin, Greengard and Ivy (7), working on dogs with a permanent fistula of the duodenum, repeatedly have obtained bilirubin and cholesterol values in the duodenal contents, following the stimulation of the gall bladder with cholecystokinin injections, that were several times higher than were the corresponding values ever found in determinations on hepatic bile obtained from normal dogs.

The above data are but a small part of the strong presumptive evidence (1) tending to prove the correctness of the assumption that the gall bladder normally evacuates its contents by way of the cystic duct. A small group of observers, however, persist in their opposition to this view. Sweet (6) has suggested that a decrease in the size of the cholecystogram is accomplished by a process of absorption of the dye by the gall bladder wall, and that the increased concentration of iodine in the duodenal contents after stimulation of the visualized gall bladder is due to a re-excretion of this absorbed dye in the hepatic bile. Sweet further maintains that all constituents of the gall bladder bile find their way to the duodenum, not by way of the cystic duct, but by a process of absorption and re-excretion in hepatic bile. Further evidence supporting his theory is the fact that most of the dye injected into an animal may eventually be recovered from a rubber bag connected to a single hepatic duct.

A consideration of the entero-hepatic circulation of tetraiodophenolphthalein offers a ready explanation of this phenomenon. Evidence has been brought forward by Johnston (2) to show that the absorption of tetraiodophenolphthalein from the gall bladder is a slow process although the question never has been investigated under the conditions of Sweet's experiment. The crucial test of Sweet's theory of gall bladder evacuation rests on whether there is an actual increase in the concentration of bilirubin, cholesterol or iodine (if tetraiodophenolphthalein is used) in the hepatic bile stream during active evacuation of the gall bladder.

TABLE II

Showing the concentration of iodine in the gall bladder 16 hours after the injection of the dye into dogs.

Dog Number	Iodine mg./c.c.
1	6.9
2	2.8
3	2.1
4	4.7
5	5.5
6	3.4
7	3.8
8	6.9
9	2.6
10	4.0
11	6.9
12	2.0
Average	4.3

METHODS

Six dogs were operated and run as "acute" experiments under barbital-ether anesthesia. The dogs were set up (sixteen hours after injecting the dye when tetraiodophenolphthalein was used) with a cannula in the common bile duct and another in the hepatic duct draining the right lobe of the liver. (In the dog,

*From the Department of Physiology and Pharmacology, Northwestern University Medical School.
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the duct draining the right lobe of the liver enters the common bile duct below the entrance of the cystic duct.) Control samples were drawn from each cannula and the animal injected with cholecystokinin. A second sample was withdrawn from each cannula after the injection and all four samples, as well as the gall bladder contents obtained at the end of the experiment, were analyzed for iodine (3), bilirubin or cholesterol as indicated in Table III. Dogs IV, V and VI were fed a fat meal two hours before the operation to ascertain if, as would be expected, the biliary constituents are higher in the common duct than in the hepatic bile stream.

RESULTS

In the first two dogs of Table III, the bile was analyzed for iodine after the injection of tetraiodophenolphthalein. Neither of these dogs showed any increase in the concentration of iodine in the hepatic bile stream during the evacuation of the gall bladder or a cholagogue response to the preparation used as estimated by the rate of flow from the hepatic duct cannula before and after injection. There was in increased iodine concentration in the bile drawn from the common duct cannula after injection as well as an augmentation in the rate of flow. Further, in Dog I the bile obtained from the gall bladder was so extremely viscus that the mere fact of its presence in the common duct cannula

TABLE III

Showing the concentrations found in the hepatic and common bile ducts before and after evacuation of the gall bladder (dog). Dogs 1-3 were starved but received cholecystokinin. Dogs 4-6 were fed fat meal in addition to cholecystokinin.

	Before Injection		After Injection		G.B.
	Hepatic Duct	C.B. Duct	Hepatic Duct	C.B. Duct	
Dog I					
Time (min.)	175	175	135	50	
Volume c.c.	0.95	0.90	0.60	2.0	
Iodine*	0.95	1.40	0.31	5.18	6.93
Dog II					
Time (min.)	30	30	35	35	
Volume c.c.	10.5	1.60	1.20	2.20	
Iodine*	1.66	1.60	1.48	2.36	4.00
Dog III					
Time (min)	50	50	30	10	
Volume c.c.	0.28	0.40	0.30	1.10	
Bilirubin†	126.0	119.0	105.1	228.1	233.0
Dog IV (fat meal)					
Time (min)	10	10	20	3	
Volume c.c.	0.28	2.8	0.26	2.9	
Bilirubin	85.3	210.0	42.0	256.0	325.7
Dog V (fat meal)					
Time (min.)	20	20	20	3	
Volume c.c.	1.0	2.1	1.1	5.8	§
Bilirubin	50.5	225.4	52.0	482.9	
Cholesterol‡	18.4	72.8	21.0	121.6	
Dog VI (fat meal)					
Time (min)	20	20	17	3	
Volume c.c.	0.2	2.3	0.25	1.5	
Bilirubin	88.5	238.0	91.5	322.3	448.6

*Iodine reported as milligrams per c.c.
†Bilirubin reported as milligrams per 100 c.c.
‡Cholesterol reported as milligrams per 100 c.c.
§This gall bladder had evacuated so completely after the injection of cholecystokinin that an accurate comparative analysis of the bile constituents could not be made.

constituted a striking tribute to the contractile power of the gall bladder. In Dog III in which the bile was analyzed for pigment alone the same results in general are tabulated. In the three animals which were fed a fat meal (Dogs IV, V and VI), however, the common duct bile was found to be much richer in biliary constituents (pigment and cholesterol) than the hepatic bile collected from the hepatic duct during the same period. The subsequent injection of cholecystokinin enriched the common duct bile still more, indicating that even under the stimulus of a fat meal (given two hours previous to the barbital anesthesia) the gall bladder does not manifest its maximum activity over a prolonged period of contraction. The bile drained from the hepatic duct was not enriched in bilirubin or cholesterol nor was the rate of flow appreciably accelerated following cholecystokinin injection. In Dog V the gall bladder had evacuated so completely after the cholecystokinin that an accurate analysis of the concentrated residue could not be made.

At least Dogs IV, V and VI have demonstrated that in the barbitalized animal during digestion there is no evidence to support the theory that gall bladder constituents are excreted in the hepatic bile and conversely leaves no explanation for the presence of higher pigment and cholesterol values in the common duct as compared with the hepatic duct unless the logical assumption is accepted that the gall bladder is slowly evacuating its contents *via* the cystic duct under the stimulus of the fat meal. Cannulation of the common bile duct also has eliminated the "milking action" of the duodenal peristalses which is of considerable importance in the evacuation of the gall bladder according to some authorities.

Experiments on more dogs were not performed because the results on the five dogs used are so striking and so readily predictable from the almost overwhelming evidence (1) in the literature that the gall bladder evacuates *via* the cystic duct. It would appear to be absolutely established that the gall bladder of man and all animals that possess a gall bladder empties *via* the cystic duct under normal conditions. At least it is believed that those who insist that the gall bladder does not so empty, have no uncontroverted evidence on which to base their claims.

Although some data have been reported on the concentration of bromine necessary to cause visualization of the gall bladder, no reports are at present available on the concentration of iodine in the visualized gall bladder of either humans or animals (1). Concentrations of iodine indicated in Table II were found in a series of 12 dogs following satisfactory visualization of the gall bladder.

CONCLUSION

The only conceivable routes by which the contents of the gall bladder may reach the common bile duct to give the results observed in this experiment are: (a) by way of the cystic duct, or (b) as Sweet suggests, by absorption from the gall bladder and re-excretion by way of the hepatic bile. It has been shown that in barbitalized dogs, the latter mechanism does not occur during evacuation of the gall bladder either by the stimulus of cholecystokinin or a fat meal. The only logical conclusion is that the gall bladder evacuates its contents by the former method: namely *via* the cystic duct.

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STUDIES ON GASTRIC MOTILITY UNDER LOW OXYGEN PRESSURES*

By

EDWARD J. VAN LIERE, M.S., Ph.D., M.D.†
MORGANTOWN, WEST VIRGINIA

ANOXEMIA, or insufficient oxygen in the blood, is found in many different diseases and it really deserves more attention than has been given to it in the past by physicians. Anoxemia is, perhaps, most commonly found in diseases of the heart and circulation; it may, however, be associated with certain anemias and also with diseases of the lungs, especially lobar pneumonia. The degree of anoxemia depends, of course, upon the severity of the disorder. In heart failure, anoxemia may be so marked that the patient actually has a bluish appearance and in certain types of pneumonia the patient also may be cyanotic and show evidence of lack of oxygen in the blood. On the other hand, it must be conceded that the body, undoubtedly, is capable of withstanding a considerable degree of anoxemia for a rather long time without showing grave manifestations. In some of the anemias, for example, the red cells may be reduced markedly in number before any striking change in the appearance of the patient is manifested. Unfortunately, there is but little mention in the literature with regard to the actual amount of oxygen in the blood in many of the diseases associated with anoxemia.

It is well known, as has been mentioned earlier, that certain cardiac disorders are associated with gastrointestinal symptoms. When the symptoms first manifest themselves at times it is not always easy to distinguish between the two conditions. This fact alone suggested that it might be worth while to study the effect of oxygen want on the stomach. Another factor which suggested the studies reported in this paper is the rapid development of airplane travel. As a consequence of this development, many people are subjected

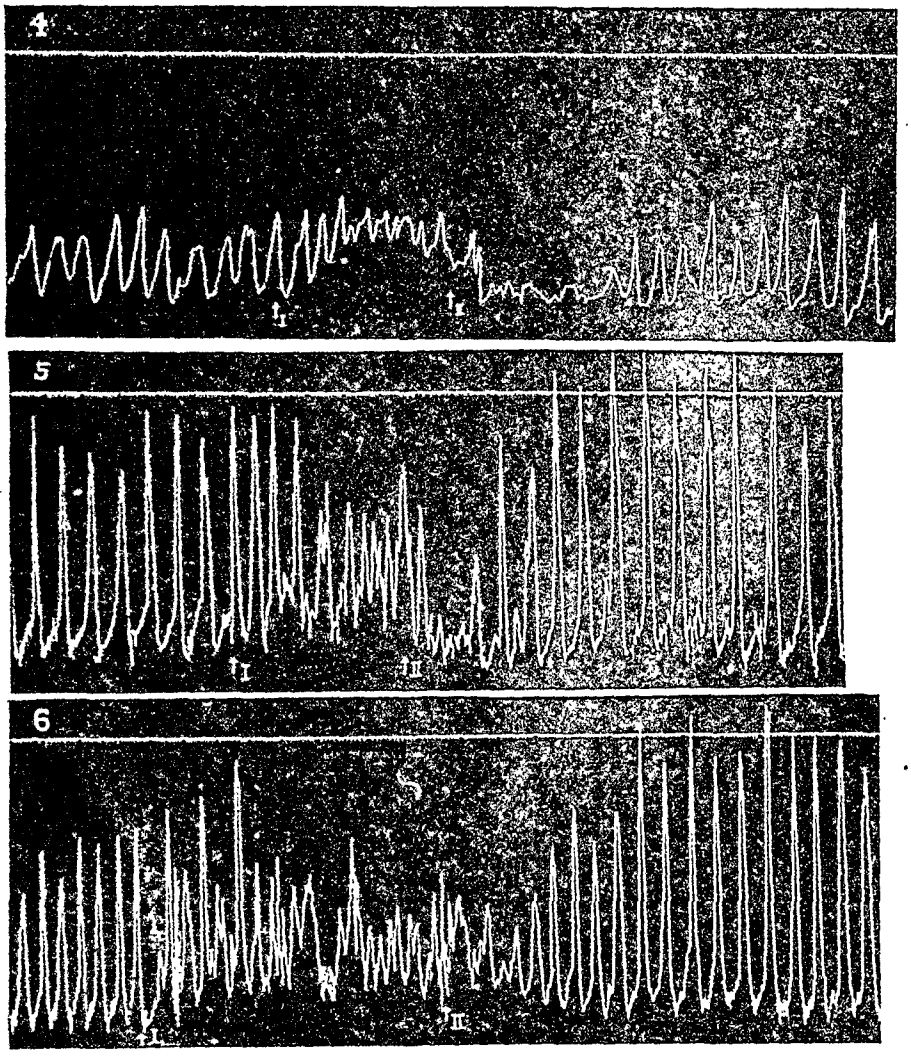


Fig. I. The effect of anoxemia on hunger contractions. At I the oxygen was changed from 20 per cent to 5 per cent and at II from 5 to 20 per cent. The time is given at 5 second intervals. Note particularly the change in height of contractions. (Reproduced by agreement with the American Journal of Physiology).

*From the Department of Physiology, West Virginia University, Morgantown, West Virginia.
†Professor of Physiology, School of Medicine, University of West Virginia.
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to anoxemia who never would have been had the airplane not been perfected. A few years ago the only persons subjected to high altitudes were the mountain climbers and the professional aviator and balloonist.

THE EFFECT OF ANOXEMIA ON HUNGER CONTRACTIONS

It was reported in some of the current literature which had to do with aviation a number of years ago, that some aviators experienced increased hunger when they made flights to high altitudes. If these reports were true, it meant that the low oxygen pressures might be capable of stimulating hunger contractions. As a result of these reports, an attempt was made to study hunger contractions under anoxemic conditions.

Hunger contractions were obtained by the usual method of inserting a small balloon into the stomach; this was inflated and connected to a water manometer which bore a suitable writing lever so that the contractions of the stomach could be recorded. After normal hunger contractions were obtained a suitable mask was put on the dog and anoxemia was administered by allowing the animal to breathe out of a rubber bag which in turn was connected to a gas machine which mixed the oxygen and nitrogen to the desired proportion (Van Liere, 1). A flutter valve was put into the circuit so that the carbon dioxide could not accumulate.

Figure 1 shows the effect of anoxemia on the hunger contractions. It will be seen that the height of the contractions were distinctly cut down. The rise in tone, however, is more apparent than real as a part of it is doubtless due to the contraction of the abdominal muscles and the subsequent rise of intra-abdominal pressure rather than the actual tonicity of the stomach. (Van Liere and Crisler) (2).

THE EFFECT OF ANOXEMIA ON DIGESTIVE PERISTALSIS

It was next thought worth while to study the effect of anoxemia on the digestive movements of the stomach. A different technique was used here.

Dogs were given barbital-sodium intravenously (200 milligrams per kilo body wt.). The abdomen was opened in the mid line, a recording apparatus or gastrograph was used (Crisler, Van Liere and Booher) (3) so that the digestive movements of the stomach could be properly recorded. After obtaining normal graphs, anoxemia was administered as has been previously described. Figure 2 shows the effect of anoxemia on the digestive peristalsis. It will be noted that the digestive peristalses were greatly decreased in height if not abolished; there was also a marked fall in tone. Some of the animals responded to 12 per cent oxygen—this really is not a severe grade of anoxemia. And in severe grades of anoxemia, such as 5 or 6 per cent, the contractions were practically abolished as Figure 2 shows.

THE EFFECT OF ANOXEMIA ON THE EMPTYING TIME OF THE STOMACH

The next obvious step in these studies was to determine the actual emptying time of the stomach. That is, if the stomach motility was lessened as previous work has shown, it was logical to believe that the emptying time of the stomach would be affected.

The normal emptying time of the stomach was determined in a group of dogs. The dogs were fed a meal consisting of 40 gm. of hamburger steak, 10 gm. of dried ground bread, and 50 c.c. of milk; 15 gm. of barium sulphate were added so that they could be examined fluoroscopically. After the normal emptying time of the stomach had been determined to our satisfaction the animals were subjected to anoxemia. This was accomplished by putting them into a large steel respiratory chamber (Van Liere, Crisler and Robinson) (4) which was capable of withstanding negative pressure. When the air pump was started a valve was so arranged so that the air could be withdrawn faster than it could enter, and as a result the animals were subjected to rarified atmosphere. By proper manipulation of the valve any desired oxygen pressure could be obtained. The air pump had a large capacity so that there was good ventilation in the tank and there was no accumulation of carbon dioxide to vitiate the experiments.

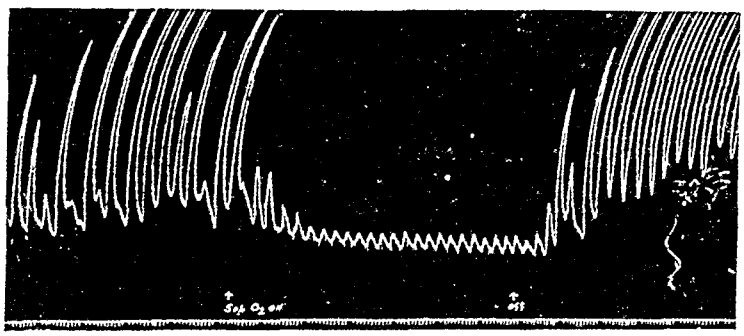


Fig. II. The effect of anoxemia on the digestive movements of the stomach. Five per cent oxygen was administered. Note the change in aplitude and the decrease in tone. (Reproduced by agreement with the American Journal of Physiology).

Figure 3 shows the effect of anoxemia on the emptying time of the stomach. It will be noted that the more severe the grade of anoxemia the longer it took the stomach to empty. It was found that the threshold for the average dog was about 8,000 feet; this corresponds to any oxygen percentage of about 15.35 and to a barometer reading of 560 millimeters of mercury. There are regions in the southwestern part of the United States which have this altitude and most of the passes which the railroads traverse over the Rocky Mountains are this high or higher.

As the chart shows, at an altitude of 14,000 feet, which is roughly the height of Pike's Peak, there was a perceptible increase in the emptying time of the stomach. In the series shown here one of the animals was rather resistant, but the other five showed an increase of several hours over their normal emptying times.

At an altitude of 20,000 feet, which corresponds to an oxygen percentage of 9.4 per cent, two of the three animals which were subjected to this height had food in their stomachs at the end of 24 hours. Higher degrees of anoxemia were not used. While 20,000 feet

seems very high it must be remembered that some of the natives of Peru live and work at an altitude of approximately 18,000 feet so that the degree of anoxemia reported was not impractical.

MECHANISM OF THE DELAYED EMPTYING TIME OF THE STOMACH

The past year or more, Dr. Crisler and I have been working on the mechanism of the delayed emptying time of the stomach under anoxemic conditions. This work has not been entirely completed but some interesting observations have been made.

The normal emptying time of a series of dogs was ascertained. These animals were then subjected to various degrees of anoxemia. When all of these data were completed they were subjected to a Rammstedt operation, that is, the pyloric muscles were cut so that these would be ineffective. After this type of operation it was found that when these dogs were subjected to anoxemia their stomachs emptied much faster than before this operation had been performed.

In another series of dogs, a posterior gastroenterostomy was performed; these experiments were subjected to the same experimental procedures as those of the Rammstedt group. The results obtained with the posterior gastroenterostomy group were more striking than even those obtained with the group first mentioned. From our data we concluded tentatively that there were at least two possible mechanisms: the first, that anoxemia was capable of producing vagospasm which would cause a pylorospasm and so hinder the feed from leaving the stomach. The second, particularly in severe grades of anoxemia, that the stomach musculature was affected by the low oxygen pressure so that the contractions were not very effective. Some more work is needed, however, to clear up certain points.

CLINICAL INTERPRETATION

As to the clinical interpretation of the various research data presented, I feel that most of the work reported here on the dog may be directly applied to man. In the case of hunger contractions, for example, it is well known that unacclimated people complain of poor appetites when subjected to high altitudes. Dr. Somervell (5) in his report of the Mt. Everest Expedition, stated that the appetite of the men at 26,700 feet was very poor and that most of their food consisted of liquids such as soup; they did, however, enjoy some pemmican. It must be remembered that these men were experienced mountain climbers, well acclimated, in splendid physical condition and for the main part, performing hard physical labor; even such men lost their zest for food. In men less physically conditioned the loss of appetite would have been, of course, infinitely more marked.

If it is true that some aviators become hungry when flying to a high altitude, the explanation may be that the low oxygen pressure causes an initial stimulation. It would seem from our data, however, that this initial stimulation would be followed by a subsequent depression. This particular phase needs more clinical investigation.

The data on the effect of anoxemia on the digestive movements and the emptying time of the stomach may be interpreted to mean that patients suffering from any disease associated with anoxemia may have a de-

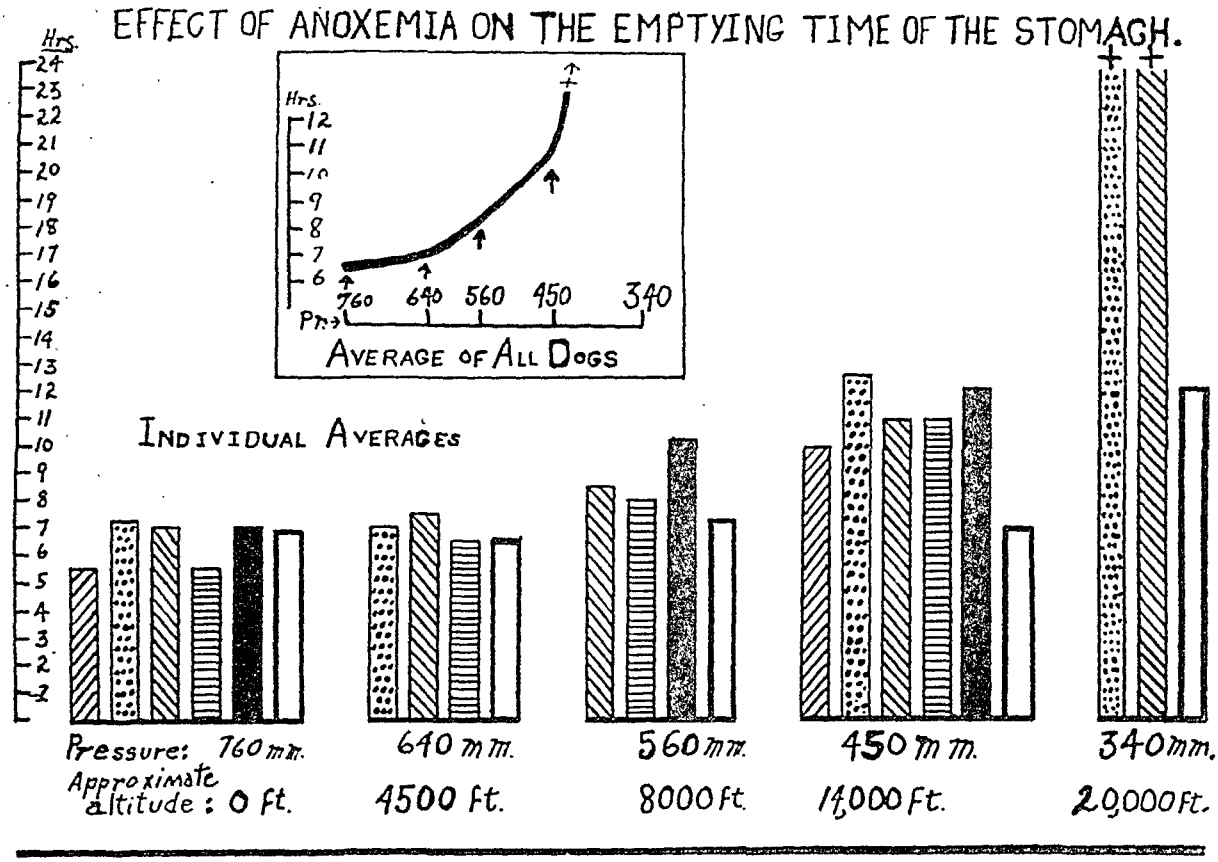


Fig. III. The effect of anoxemia on the emptying time of the stomach in 6 animals. Each animal is indicated by a specific shading. Note that all animals were not run at all the various pressures. (Reproduced by agreement with the Archives of Internal Medicine).

layed emptying time of the stomach. It is quite possible man may show even greater susceptibility to anoxemia than did the dog. The reason for this statement is that in no case did we observe retching or vomiting in the dog when it was subjected to anoxemia and in the past four years many animals have been used. I believe that it is generally conceded that most people are apt to become ill if they ascend an appreciable height. It is stated (Air Medical Service, 1919) that unacclimatized people are often sick at 10,000 feet and that many people are sick at 14,000 feet and that practically everyone becomes sick at 18,000 feet. Certainly many tourists become nauseated, vomit and show other signs of mountain sickness at the top of Pike's Peak. It is true that these people are often physically active which would, of course, tend to use their oxygen and make them more anoxemic. In the experiments quoted in the dog, on the other hand, we were not dealing with any physical exercise. The dogs remained very quiet when they were in the respiratory chamber and if they were kept in there a long time they would often go to sleep for a time.

I believe that our experimental work has emphasized the importance of prescribing easily digestible food and food that will leave the stomach quickly in cases of disease associated with anoxemia. It will be recalled that animals subjected to what may be termed moderate grades of anoxemia showed a delay of several hours in the emptying time of their stomachs. It is doubtless true that the physician has learned to prescribe the proper kind of food as he found by experience that such patients as mentioned above could not handle, so to speak, heavy diets. I feel, however, that the data presented in this paper furnish controlled experimental evidence to prove this beyond any question of doubt.

In this review, emphasis has been laid on high altitudes, but it is hardly necessary to reiterate that the results are applicable to any disease which is associated with anoxemia. At the present time, work is going on using man as a subject and further work is in progress on the various mechanisms involved.

ACKNOWLEDGMENT

I wish to acknowledge with thanks the courtesy rendered me by the managing editors of the American Journal of Physiology and the Archives of Internal Medicine for their consent to use certain graphs and charts which originally appeared in their publications.

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A STUDY OF THE ABSORPTION OF DEXTROSE AND WATER FROM CHRONIC ISOLATED LOOPS OF THE COLON*

By

PHILIP H. MOORE, M.D.

and

G. E. BURGET, Ph.D.

PORTLAND, OREGON

MUCH has been written on the efficacy of introducing fluids and nutrient substances into the colon. The exact date on which this procedure was first initiated is uncertain, but the use of such enemas as a source of energy and fluid has been handed down to us as a time-proven therapeutic method. This procedure is used in some form in almost all hospitals. In spite of the long period of use, it has, until recently, been upon a more or less empirical basis. Some clinicians and investigators have lauded the use of the addition of various chemicals, such as sodium chloride and sodium bicarbonate, with the object of speeding up the absorption of water and sugar. The per centum of sugar solutions used exhibits wide variations.

While we admit that conclusions as to the efficacy of the nutrient enema cannot be established by one set of experiments, the following studies are presented with the hope that they will add to the evidence which already has been recorded.

The feasibility of using the chronic closed-loop of the dog's small intestine for the study of absorption amply has been shown.[1,2,3,4,5] Using a technique similar in major respects to that described by Martzloff and Burget,[3] we have succeeded in making chronic closed-loops of the colon in twenty-five dogs. Five animals were lost following the operation; twenty made rapid recovery and became satisfactory experimental subjects. One animal (Number 9), has been used for more than one year with no change in her normal condition or in the absorbing qualities of the loop. Grossly, the mucosa appears normal even after long periods of time elapsed between the date of operation and the sacrifice. A loop removed three and one-half months after operation was studied in microsections. There were no demonstrable changes in the mucosa but the muscular layers were found to be thinner than those of the intact bowel.

The closed-loop permits absorption experiments on healthy dogs with a minimum of trauma and without the use of narcotics. This method avoids many objectionable factors encountered in most of the previous work. It allows for controlled analysis of the substances tested and removes the variable factors of regurgitation into the ileum and contamination by fecal material.

Review of literature. In reviewing the literature, roughly we may divide the experiments into two groups, (1) those performed on man and (2) those performed on experimental animals.

The experiments on man may be segregated into the following groups: Levi,[9] Bengel[10] and Arnheim[14] report experiments on diabetic patients. Tallerman,[7] Pressman,[10] Scott and Zweighaft,[11] and de Takats[20]

*From the Department of Physiology, University of Oregon Medical School.
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studied colonic absorption of dextrose relying upon the changes in blood sugar as evidence. The changes in respiratory quotient as proof of absorption of sugar were used by Reach,[6] Rubino and Varela,[8] and Carpenter,[15] while the "washout" method was utilized by Halasz,[16] Mutch and Ryffel,[17] Boyd and Robertson,[18] Zehmisch,[13] and Deucher.[12] Perusse[21] presents some interesting findings in both man and dog.

These methods, however, are subject to adverse criticism. Previous work in this laboratory[22] would seem to indicate that changes in systemic blood sugar are not indications of dextrose absorption, at least not when the amount absorbed is small. Smith[23] reports that diabetic patients will show marked variation in the readiness with which liver glycogen may become mobilized in response to nervous stimulation and to mechanical pressure changes in the intestinal tract. The sensitive patient can show a slight blood sugar rise from the mere insertion of a rectal tube, with a more marked increase in blood sugar occurring later if the amount of solution introduced into the rectum is sufficient to cause pressure within the lumen of the gut. Such increases in the blood sugar do not indicate, necessarily, that glucose is absorbed. In fact, slight increases in blood sugar may appear when distilled water or simple saline solution is injected into the rectum in small amounts.[31] The very slight increases in respiratory quotients that have been reported might be influenced by the reversal change to glycogen synthesis which could follow the increase in blood sugar from stimulation.[10] Brodie[24] and his collaborators report that distilled water instilled into the bowel will cause increased oxygen consumption. Two pitfalls that have not always been taken into consideration in the above work are regurgitation into the ileum[10] and bacterial action.

Hari and Halasz,[25] Ornstein,[26] Franke and Wagner,[27] McNealy and Willems,[28 29] Varela and Rubino,[30] and Ebeling[31] have reported the results of experiments upon the dog. All the work by these men is subject to the criticism that an anesthetic was used and the gut more or less was traumatized in carrying out the experiments. Ravdin[38] and his associates, however, used a Thiry fistula as modified by Johnston.[39] This would seem to be an improvement over the previous methods.

In order to arrive at the facts concerning absorption from the colon, the investigator should not overlook the following: (1) regurgitation of material from the colon into the ileum is a constant possibility in judging absorption from the colon where the intestinal tract is intact; (2) the peripheral blood sugar probably is not an accurate indication of absorption of dextrose from the colon; (3) changes in the respiratory quotient are not reliable as evidence of absorption; (4) varying percentages of dextrose will influence the absorption of water and probably that of dextrose; (5) bacterial action on the injected sugar should be determined, especially where the absorption period exceeds one hour, (6) and finally, narcotization and visceral traumata have a retarding influence upon the absorption of both water and dextrose in experimental investigations on laboratory animals.

METHODS

Operative technique. Dogs weighing 35 to 40 pounds, preferably between the ages of 1 and 3 years and in good health, were selected for the operation. The dogs were starved for twenty-four hours and given an enema of soap and water immediately before the operation. At least one pint of solution should be used, since it is extremely important to have the colon empty of fecal material. After expulsion of the enema, routinely we gave a hypodermic injection of morphine (¼ grain) and atropine (1/100 grain). Surgical asepsis was maintained throughout the operation. Since the technique of the operation fundamentally is the same as that given by Martzloff and Burget[7] for loops of small intestine, only those points of difference when the large intestine is used will be cited. A left rectus incision is made 7-8 cm. long, parallel to and 2.5 cm. from the *linea alba*, and so situated that the umbilicus marks the midpoint of the opening. The descending colon is located and carefully drawn through the incision.

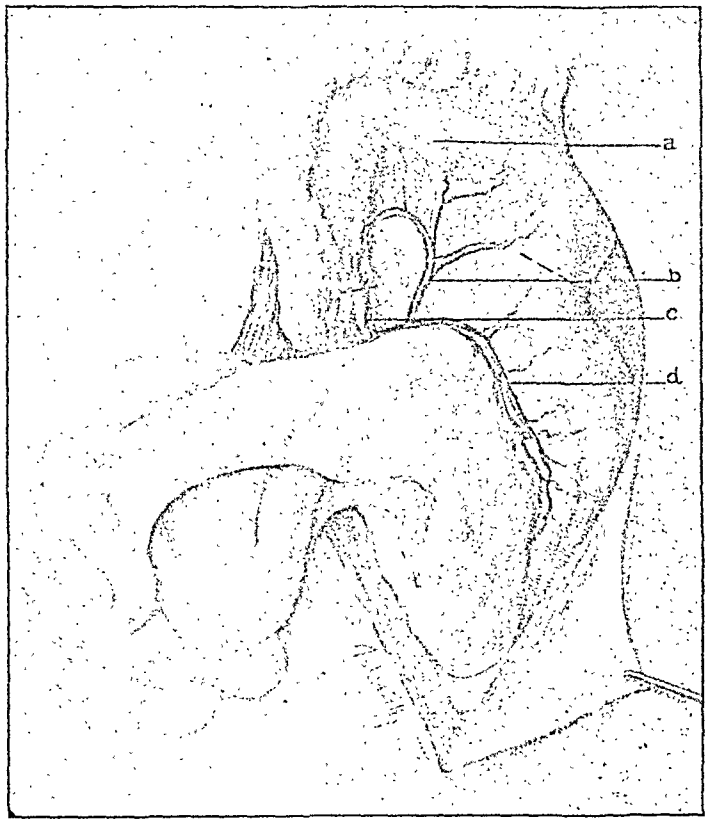


Fig. 1. a—transverse colon; b—rt. colic vessels; c—ileo-colic vessels; d—median colic vessels. Clamps placed at dotted lines.

(The descending portion of the dog's colon is supplied by the median colic artery which runs parallel to the large intestine. The transverse colon is 8 to 12 cm. in length and is supplied by the right colic artery. The short ascending portion is supplied by the ileo-colic artery.) The transverse portion is isolated by clamps and separated from the remaining large intestine. The blood supply and the nerves to this segment remain intact and, in the subsequent handling and attachment of the loop to the anterior abdominal wall, great care should be taken to avoid torsion, undue pull or relations which later may obstruct the blood supply. Before clamping or in any way injuring the intestine, a thorough inspection of the colon should be made. (1) *It should be free of fecal material.* If the fecal material has not been entirely expelled and is not hard, one may carefully milk this material distally until the desired segment is empty. Severe trauma should be avoided, since it results in constriction of the powerful muscle coats and makes manipulation exceedingly difficult or impossible. (2) *The transverse portion to be used should be at least 10 cm. long in the relaxed state.* If shorter than this it will result in a loop so small that it is impractical for later use. (3) *The mesentery to the transverse colon should be of sufficient length to allow for attachments of the loop to the anterior body wall without tension on the attachments or mesenteric pedicle.* (4) Since the caecum is attached by mesentery to the peritoneal surface of the posterior abdominal wall, *a free transverse portion 4 cm. in length is necessary for anastomosis with the descending colon.* If the above mentioned conditions are not all met, we have considered it advisable to close up the animal and to select another. We have found only 3 dogs in 28 in which we decided against the completion of the operation.

The attachment to the anterior abdominal wall is made with the long axis of the loop parallel to and near the mid-line, and the anastomosed colon kept lateral to the loop and its mesentery. The only practical difficulty we have had is at this point. Either because of the more powerful contractions of the large bowel or because adhesions are formed with greater difficulty, the large bowel loop is much more difficult to keep snugly attached to the abdominal wall. Very little difficulty is experienced in maintaining the attachment of the loop of the small intestine. In attaching the loop of large bowel, traumatization of the sur-

faces to be apposed should be thorough, and the placing of single interrupted sutures in a slightly staggered fashion so as to bring a broad surface of intestine against the peritoneum seems of value. Attachments may be satisfactory for several weeks. At this time a stretching of the attaching adhesions may be noted and it may be so extreme that a reattachment becomes necessary.

Postoperative care is, in most cases, very simple. The dog is allowed water four to five hours after the operation. Small quantities of ground meat, or similar low-residue food, is given forty-eight hours after the operation. Portions of low-residue food are given on the fourth day and the usual diet resumed at the end of one week. Straining in an attempt to defecate, stretching or vomiting usually will indicate loop distention.

The washing of the loop and the injection of material to be analyzed are very simple. The abdominal wall is shaved over the point of loop attachment and cleansed with 70 per cent alcohol. A 20 c.c. glass syringe is fitted with a 19 gauge needle, one and one-half inches long, and both are sterilized by boiling. The needle is inserted into the loop with a quick thrust, and sterile 0.9 per cent sodium chloride at body temperature is injected. The injection of salt solution has two purposes: first, to verify the entrance of the needle into the loop; and second, to wash out any accumulated mucosal debris. After the first few experiments on any given animal, the loops of colon usually remain clean, and very little foreign material is withdrawn. (This is in marked contrast to the loops of the small intestine. These are liable to much greater variation in activity and consequently

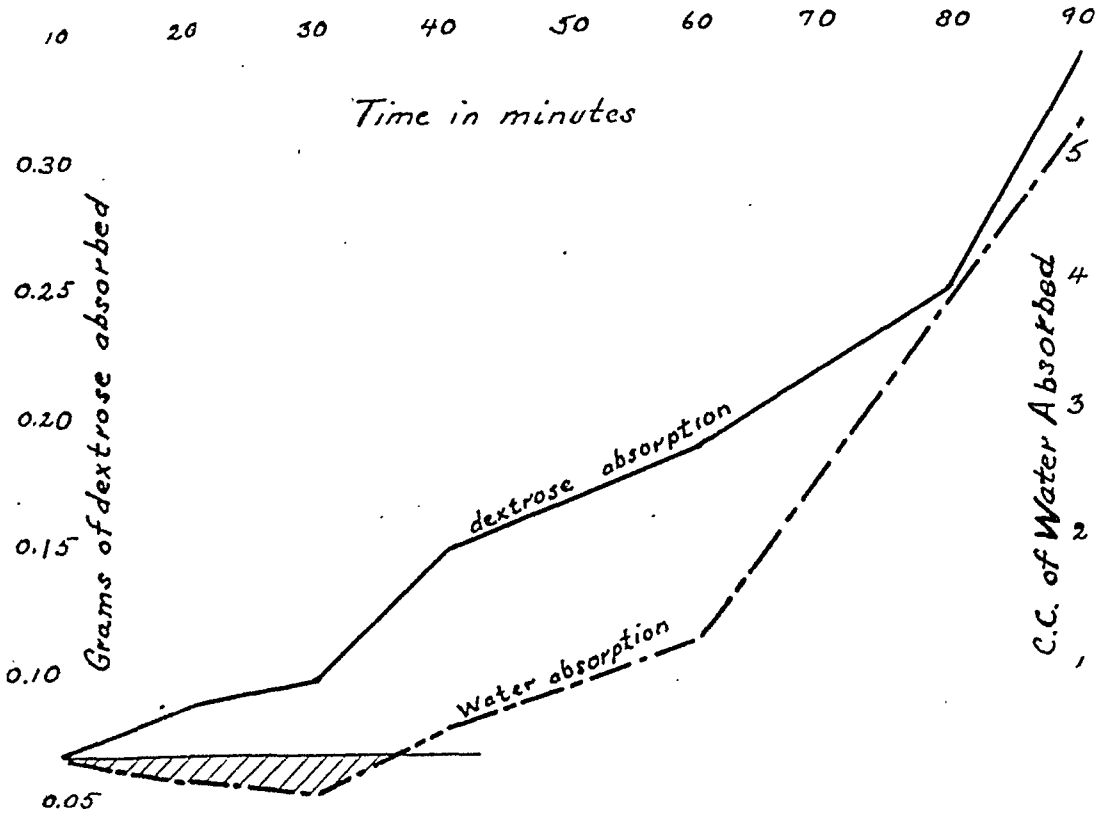


Chart 1. The amount of dextrose and water absorbed for different time-intervals from 10 c.c. of a 5 per cent dextrose solution. The curve for water absorption lying below the cross-hatch area represents a period when there was an influx of fluid into the loop. When 10 c.c. of a solution is injected and aspiration is immediate the actual amount withdrawn averages 9.6 c.c. Any amount in excess of 9.6 c.c. is interpreted as an influx of fluid.

Postoperative aspiration was necessary in six of twenty-five dogs operated upon. Early in the series, we lost two dogs by rupture of distended, unaspirated loops. Both dogs died within six days of the operation. In the absence of the above symptoms, aspiration is not advisable since the loop may be disturbed in its attachment before adhesions are organized.

According to the general condition of the animal, actual experimental work is begun ten to fourteen days after the operation. The care of the dogs from this time on is similar to that of any normal animal. Continued accumulation of fluid after postoperative healing is complete, probably always means an obstruction to the venous return from the loop. One dog in our series was discarded because of repeated loop distention brought about by an obstruction to the venous return from the loop.

Determination of sugar absorbed. Pfanstiehl dextrose, having a specific rotation of 52.5 degrees at 20 degrees C., accurately was weighed and dissolved in distilled water. These solutions were diluted to a standard volume in accurate volumetric flasks. As a further check on the accuracy of the solutions each new sugar solution was checked by the same method and measuring apparatus as was used in analysis of the fluid withdrawn from the loops. Where sodium bicarbonate or sodium chloride was added, the amount was accurately weighed.

are much harder to keep in a usable condition.) The loop is washed and completely emptied of the fluid used for washing. The desired amount of sugar solution then is accurately measured by pipette and placed in a syringe for injecting. The syringe used for the sugar injection is then rinsed out with distilled water which is saved and analyzed with the unabsorbed sugar aspirated from the loop. Originally we analyzed the sugar rinsed from the injection syringe separately, but found the amount to be less than 0.05 gm. It was therefore added to the withdrawn solution for determination. This gives a more accurate estimation of the amount absorbed and eliminates the small, variable amount which might have been lost by adherence to the syringe used for injecting.

The dog then is released from the table and allowed to pursue its normal inclinations for the period allowed for absorption. At the end of this period, the fluid containing the unabsorbed material is withdrawn and the amount of fluid measured. The remaining sugar in the loop is washed out by injecting and withdrawing three 15 c.c. quantities of normal saline.

In checking for the accuracy of the above procedure we have injected a known quantity of sugar, immediately withdrawn it and determined the amount of sugar aspirated. The error has been within 3 per cent.

The aspirated fluid, plus the syringe and loop washings, is

diluted to a standard volume of 100 c.c. in a volumetric flask. After the proper dilution of this fluid it is analyzed by the Shaffer-Hartman method as modified by Haskins and Holbrook.[32,33] Repeated checks on known solutions have shown that in the dilutions used the small amounts of protein, sodium chloride or sodium bicarbonate do not affect the accuracy of the method in determining the per cent of contained dextrose. (This method may be used for the analysis of levulose and galactose by adding 10 per cent to the amount of dextrose which corresponds to the titration figure.[4,5] It is not accurate, however, for the determination of mannose.[34])

The amount of sugar as determined above, is subtracted from the known amount injected and the difference recorded as sugar absorption.

The determination of sodium chloride was by the method of Volhard.[35]

EXPERIMENTS

The first series of 29 experiments (Table 1) was performed in an attempt to study the rate of absorption from a solution approximately isotonic with blood and tissue fluids. In Chart 1 is shown the corresponding amount of water absorption.

TABLE I

Absorption of dextrose after injection of 10 c.c. of a 5% solution.

Time in Minutes	Grams Absorbed				
	Dog 9	Dog 12	Dog 17	Dog 18	Average
10	0.07	0.10	0.05	0.08	0.07
20	0.09	0.10	0.09	0.09	0.09
30		0.12	0.09	0.08	0.10
40	0.08	0.23		0.14	0.15
60	0.12	0.22	0.14	0.30	0.19
90	0.24	0.31		0.33	0.29

When 10 c.c. of a 20 per cent concentration of sugar was used the amount of fluid withdrawn at the end of a one-hour period was approximately double the amount injected. Absorption of dextrose under these conditions is shown in Table 2.

TABLE II

Grams of dextrose absorbed in one hour following injection of 10 c.c. of a 20% solution.

Dog 6	Dog 7	Dog 9	Dog 10	Dog 12
0.75	1.34	0.39	0.38	0.52
0.76	1.30	0.35	0.45	0.48
0.83	1.57	0.32	0.56	0.51
0.58	1.20	0.32	0.72	0.32
0.78		0.36	0.73	0.34
		0.39	0.77	
		0.39		
		0.29		
		0.36		
Average 0.74	1.35	0.35	0.60	0.43

Twenty-five experiments were performed using 10 c.c. of a 10 per cent solution of dextrose. The resulting absorption in a given loop on repeated experiments was remarkably constant as demonstrated by Table 3. The average amount of fluid withdrawn at the end of one hour was 12 c.c. These animals exhibited no disturbances from distention of the loop. When a more concentrated solution was injected, the greater influx of fluid sometimes caused discomfort or even vomiting from over distention.

The absorption of dextrose and water from 10 c.c. of a solution containing 2.5 per cent dextrose and 0.45 per cent sodium chloride in one hour was tested. This solution approximately is isotonic with blood and tissue fluids. Ten experiments were performed. The total amount of sugar injected was 0.25 gm. The average amount of sugar absorbed in dog number 9 was 0.09 gm.; in dog number 12, 0.10 gm., and in dog number 18, 0.11 gm. This is an average of 0.10 gm. or 40 per cent of the injected sugar.

TABLE III

Grams of glucose absorbed one hour from colon loop following injection of 10 c.c. of a 10% solution.

Dog 9	Dog 12	Dog 18	Dog 21	Dog 22
0.19	0.20	0.27	0.22	0.24
0.19	0.25	0.24	0.22	0.20
0.20	0.22	0.27	0.19	0.22
0.18		0.27	0.21	0.21
0.19		0.25	0.20	
0.18		0.22	0.18	
Average 0.20	0.23	0.25	0.22	0.22

The absorption of dextrose and water from a solution containing 5 per cent dextrose and 1.5 per cent sodium bicarbonate was also investigated. A total of 25 experiments were performed (Table 4).

TABLE IV

Grams of dextrose absorbed from 10 c.c. of a solution containing 5 per cent dextrose and 1.5 per cent sodium bicarbonate in a one-hour period.

	Dog 9	Dog 18	Dog 21	Dog 22
Gms. Dextrose Absorbed	0.15	0.24	0.13	0.17
	0.11	0.15	0.12	0.17
	0.10	0.22	0.20	0.15
	0.10	0.19	0.12	0.15
	0.12	0.17	0.12	0.14
	0.10	0.17	0.12	
		0.16		
Average	0.11	0.19	0.13	0.16

The average absorption of dextrose for the four dogs was 0.15 gm. The average amount of fluid withdrawn was 16 c.c. In contrast to this an average of 0.19 gm. of dextrose was absorbed where 5 per cent dextrose in water was used and 8.6 c.c. fluid was withdrawn (see Table 1 and Chart 1).

When 10 c.c. of a 0.9 per cent solution of sodium chloride was injected and left for one hour, an average of 8 c.c. of the fluid and 80 per cent of the sodium chloride injected were absorbed. Analysis for sodium chloride in the sample withdrawn gave percentages varying from 0.6 to 1.0 per cent, with an average very close to 0.9 per cent.

BLOOD SUGAR FROM COLONIC LOOPS AND SYSTEMIC BLOOD

Method: The dogs were placed on a table and the abdomen shaved. Blood was then drawn from the heart, oxalated and saved for sugar analysis. Ten to 15 c.c. of 10 per cent dextrose was injected into the loop and the time recorded. Forty minutes from the time of the injection the animal was given ether anesthesia and prepared for a laparotomy. The abdomen was opened under strict asepsis, through a left rectus incision, and blood drawn from the vein draining the colon loop. Blood was drawn almost immediately from the heart. Both specimens were oxalated to prevent clotting and these were kept for analysis. The time-interval between injection of sugar into the colon loop, and aspiration of blood from the loop vein and the heart was one hour. The incision was then closed and the animal placed in a warm room to recover. The entire operative time was less than thirty-five minutes.

A protein-free filtrate of the blood samples was then prepared by the method of Folin and Wu,[36] and the blood sugar determined by the Shaffer-Hartman method as modified by Haskins and Holbrook.[32,33] The milligrams of blood sugar corresponding to the titration figure were read from the table published by Haskins.[37]

The blood sugar, in the blood withdrawn from the colonic-loop vein, always exceeded that found in the blood drawn simultaneously from the heart. The difference averaged 8 milligrams per 100 c.c. of blood. A point of much interest is the change noted in blood sugar during ether anesthesia. In nine dogs, in which we determined the blood sugar during anesthesia, we found a doubling of the blood sugar per cent in eight animals. In one animal there was no increase in blood sugar with the anesthesia.

Although we have felt that the amount of dextrose lost by bacterial action is insignificant for a one-hour period, we performed experiments to determine this. Ten c.c. of 10 per cent dextrose was injected and then withdrawn. By this procedure the bacteria of the colon loop were mixed with the sugar solution. The sugar content in a sample of the aspirated fluid was immediately determined. The remainder was placed in a loosely stoppered flask, incubated at 37.5 degrees C. for one hour and the sugar content then determined. We were unable to detect any loss of sugar by bacterial action, since the percentages of sugar in the two samples, taken before and after incubation, were identical.

DISCUSSION AND INTERPRETATION OF RESULTS

Dextrose absorption. Before beginning a long series of experiments on dextrose absorption we wished to convince ourselves of actual absorption by the mucosa of the colon. We have, as previously stated, minimized all the sources of error known to us. In order to determine whether there was actual absorption the first series of experiments was performed. By referring to Table 1 and Chart 1, it will be noted that an average of 0.07 grams of dextrose had disappeared in 10 minutes, and that the amount of sugar lost steadily increased to 0.29 gms. or 58 per cent of the injected sugar at the end of one and one-half hours. The rate of water absorption bears little relation to this, especially for the periods less than forty minutes. If diffusion is the only factor, the rates of water absorption and sugar diffusion should be comparable. Whereas, water absorption was not positive until the forty-minute period, a definite and steadily increasing sugar loss was noted at the end of a ten-minute period. This is even more significant when one considers that the dextrose solution approximately was isotonic with the blood and tissue fluids. We considered these findings as indicative of actual absorption by the chronic closed colon loop.

In a consideration of the absorption of dextrose from 10 c.c. of a 20 per cent solution, we find that the average for 29 experiments on five dogs was 0.49 gms., or approximately 25 per cent of the injected sugar. It is apparent that the per cent of the injected sugar absorbed is much less than when a 5 per cent solution was used. The reasons for this may be several. The marked hypertonicity may have inhibited absorption by physical means of osmotic pressure relations; the capacity of the mucosal surface for absorption may have been exceeded; the blood supply to the loop may have been embarrassed by distention or there may have been an inhibitory effect exercised on the mucosal cells. From the standpoint of absorption in grams it should be noted that 0.49 gms. of the 2 gms. injected was absorbed from the 20 per cent solution as compared to 0.29 gms. from a 5 per cent solution. Ravdin[39] has reported similar observations regarding the relation between the concentration of the sugar solution and the amount absorbed.

When 10 c.c. of a 10 per cent solution was injected, the average absorption in 25 experiments was approximately 0.22 gms. or 22 per cent of the injected sugar. This percentage of absorption approximately is the same as for a 20 per cent solution. The amounts absorbed from the 10 per cent solution in single experiments were remarkably constant. The highest and lowest figures for any given animal did not differ by more than 0.05 gm. All the other solutions, but especially the 20 per cent dextrose solution, showed less constancy in the absorption rates. This fact may indicate that, when considering sugar absorption alone, this volume and percentage of dextrose may be the least objectionable for studying the comparative absorption rates of various sugars.

The presence of 0.45 per cent sodium chloride in a 2.5 per cent solution of dextrose did not seem to increase the percentage of sugar absorption. Forty per cent (0.10 gm.) of the dextrose was absorbed in a one-hour period as compared with 58 per cent of the 5 per cent solution of dextrose in water. Both of these solutions approximately are isotonic with 0.9 per cent saline.

One and one-half per cent sodium bicarbonate in a 5 per cent dextrose solution resulted in a lowered rate of dextrose absorption. In 25 experiments an average of 0.15 gm., 30 per cent of the amount injected, was absorbed in one hour. Forty per cent of the saline-dextrose solution and 58 per cent of the 5 per cent dextrose solution were absorbed in the same period of time.

In summarizing, we may state that: (1) the optimal percentage of dextrose solution for absorption of dextrose probably lies somewhere between 5 and 10 per cent; (2) the absorption from a 20 per cent solution is higher in grams absorbed but lower as regards percentage of sugar injected than for any other solutions tested; (3) the amount of absorption varied considerably when a 20 per cent solution was used; (4) the addition of sodium chloride in isotonic solutions apparently does not facilitate dextrose absorption, and finally, (5) that the addition of small quantities of sodium bicarbonate to a 5 per cent sugar solution resulted in a diminished rate of sugar absorption.

Water absorption. The effects of dextrose, of sodium chloride and of sodium bicarbonate on the rate of water absorption and on the influx of fluid into the lumen of the chronic closed colon loop have been studied. Chart 1 shows that there is no definite correlation between the amounts of sugar and water absorbed from a 5 per cent solution of dextrose in water. Whereas, there is a positive absorption of dextrose within ten minutes following injection, a definite water absorption is not evident until almost forty minutes following injection. A point of major importance, however, is that with this concentration of dextrose we were unable to detect more than a slight influx of fluid into the loop at any interval in the absorption period, and that after the forty-minute period the absorption of fluid proceeded at a fairly constant rate. Approximately 50 per cent of the injected fluid was absorbed in the ninety-minute interval.

When 10 c.c. of a 20 per cent solution of dextrose in water was injected and aspirated in one hour, not only was no water absorbed but 10 to 15 c.c. of fluid had entered the loop in an attempt to dilute the hypertonic sugar solution. In spite of this influx of fluid positive absorption of sugar evidently occurred.

At the end of a one-hour absorption period an average of 12 c.c. of fluid was withdrawn after the injection of 10 c.c. of a 10 per cent water solution of dextrose. As previously stated, the animals showed no signs of loop distention during the absorption period and, although an average increase in fluid of 2 c.c. was

found at the end of the one-hour period, it is evident that the influx of fluid was never large enough to cause marked distention of the loop. In this series of experiments we again found evidence of dextrose absorption in spite of influx of fluid.

Since it had been reported by different investigators that the addition of sodium chloride to an isotonic solution of dextrose might influence the rate of water and sugar absorption, we performed a series of experiments injecting a solution containing 2.5 per cent dextrose and 0.45 per cent sodium chloride. If the relative osmotic pressure of the injected fluid and tissue fluids were the only factor influencing the absorption of water by the mucosa, we might expect the rate of fluid absorption to be similar to that from a 5 per cent solution of dextrose in water, since both solutions are theoretically isotonic with the blood and tissue fluids. This did not prove to be the case. The amount of water absorbed in one hour from a 5 per cent solution of dextrose in water was about 1.5 c.c. in contrast to an average of 7 c.c. absorbed in one hour from the dextrose-saline solution. Either the presence of the sodium chloride hastens water absorption, or the increased amount of dextrose in the 5 per cent water solution delayed the fluid absorption. This is even more significant when we note that the relative percentage of the sugar absorbed was approximately the same in both instances.

The absorption of water from a solution containing 5 per cent of dextrose and 1.5 per cent sodium bicarbonate was equally striking. At the end of a one-hour absorption period, an average of 16 c.c. of fluid was withdrawn after the previous injection of 10 c.c. of the dextrose-bicarbonate solution. The influx of fluid here almost equaled that found when a 20 per cent dextrose solution was injected. We know that the osmotic pressure exerted by any fluid is determined by the number of molecules and ions in the solution, that dextrose does not ionize and that sodium bicarbonate does, and finally, that the molecular weights of the two substances are markedly different (84.01 for sodium bicarbonate and 198.11 for dextrose). We might use these facts to explain the marked increase in fluid influx with the addition of such a small quantity of sodium bicarbonate, but the results obtained by the addition of a small quantity of sodium chloride, a highly ionized salt with a low molecular weight (58.45), were exactly the opposite as regards the fluid balance. In the latter case fluid absorption was comparatively rapid. We are forced to believe that the difference is not due to changes in relative osmotic pressures but to some effect which the substances have on the activity of the colon mucosa.

It was decided to test the rate of water absorption from a third solution, isotonic with the blood and tissue fluids, in which no dextrose was present. Ten c.c. of a 0.9 per cent solution of sodium chloride was injected and aspirated in one hour. Eighty per cent or 8 c.c. of the injected fluid was absorbed, compared to 5 c.c. from a 5 per cent solution of dextrose and 7 c.c. from a solution containing 2.5 per cent dextrose and 0.45 per cent sodium chloride. If osmotic pressure were the only factor we would expect water absorption to be greatest from the 5 per cent solution of dextrose and least from a 0.9 per cent solution of sodium chloride. The exact reverse was found. It would seem that some influence of dextrose on the activity of mucosal cells tends to slow the absorption of water.

As regards the absorption of sodium chloride from a 0.9 per cent sodium chloride solution, the following results were found. The percentage of sodium chloride in the aspirated sample was approximately the same as that of the injected fluid, i. e., 0.9 per cent. This would indicate that the absorption of sodium chloride is comparable to that of water.

In summarizing the above points it would seem that: (1) any solution containing 10 per cent or more dextrose will actually dehydrate the tissues, by causing an influx of fluid into the gut; (2) the addition of small quantities of sodium bicarbonate (1.5 per cent) to a 5 per cent dextrose will likewise result in an influx of fluid into the gut; (3) small quantities of fluid (1-2 c.c.) are absorbed in one hour from 10 c.c. of a 5 per cent solution of dextrose; (4) 7 c.c. of fluid are absorbed in one hour from 10 c.c. of a solution of 2.5 per cent dextrose and 0.45 per cent sodium chloride; (5) 8 c.c. of fluid are absorbed in a similar time from 10 c.c. of a 0.9 per cent sodium chloride; (6) dextrose, in any percentage, may inhibit the rate of water absorption, and (7) finally, osmotic pressure relationships do not seem to explain the differences in absorption rate.

Relation of loop size to amount of absorption. This relationship has been interesting and very constant. Observations during operation, while experimenting and at autopsy on dogs numbers 6, 7, 9, 10, 17, 18, 21 and 22 indicate a close correlation between loop sizes and absorption rates. The amount of water and dextrose absorption is directly proportional to the mucosal surface area of the loop.

Comparison of absorption in the lower ileum and in the colon. In order to make a comparison of the findings at the two levels Table 5 is reproduced from a paper previously published by Burget, Moore and Lloyd.[4]

TABLE V

Results of repeated experiments on individual dogs expressed as grams of dextrose absorbed by closed ileal loops in one hour from 10 c.c. of a 20 per cent solution of sugar.

	Dog 61	Dog 131	Dog 132	Dog 135
	0.98 0.97 0.99	1.01 0.97 0.85 0.77 0.93	1.38 1.11 0.74 0.75 0.65	1.03 0.97 0.72 0.73
Average	0.98	0.90	0.91	0.86

The average amount of dextrose absorbed for the four dogs is 0.91 gms. Comparing the absorption in one hour from 10 c.c. of a 20 per cent dextrose solution in the colon (Table 2) we find that the absorption rate is much higher in the ileum. An average of 0.49 gms. was absorbed by the colon loop and 0.91 gms. from the ileal loop, the colon loop absorbing 53 per cent of the amount absorbed by the ileal loop.

In comparing the relative absorption from 10 c.c. of a 10 per cent solution we find that the low ileal loops absorbed an average of 0.52 gms.[4] as compared with 0.22 gms. by the colon loop, as reported in this paper (Table 3). The colon loop absorbed 41.5 per cent as much dextrose as the ileal loop from an identical solution in the same time period.

The above comparison would seem to indicate that the absorption of dextrose, under these conditions, is twice as rapid in the lower ileum as compared with the transverse colon in the dog.

In comparing the relative influx of fluids, when these two solutions were used, we find that when 10 c.c. of a 20 per cent dextrose was injected that the average influx was 19 c.c. in the low ileal loop and about 12 c.c. in the colon loop. With the 10 per cent solution the increase was 9 c.c. for the ileal and 2 c.c. in the colon loop.

Either water is absorbed faster by the colon or there is much greater initial influx of fluid into the ileal loop. The amount of fluid increase in the ileal loops varied from 6 to 30 c.c., whereas the influx into the colon loops was very constant. The small intestine must be much more sensitive to changes in osmotic relationship and to irritating or inhibiting factors. This relative stability of the colon has been noted in all our experimental studies on absorption.

Evidence of absorption as indicated by simultaneous analysis of the blood sugar from loop and systemic blood. As final evidence of positive absorption, we again draw attention to the experiments where the blood sugar from the loop veins was compared with that of heart blood during an absorption period. As previously stated, we have found an increase in the blood sugar from ileal loop veins as compared with that from the heart and demonstrated this difference to be due to levulose absorbed from the ileal loop.[5] Seven experiments were performed. In the experiments reported in this paper, we found that the blood sugar from the colon loop veins exceeded the amount present in the heart's blood by approximately 0.008 gm. Sugar must have been entering the mesenteric veins from the loop. This small amount of sugar was probably removed by the liver.

In interpreting the conclusions given below, and in the application of these interpretations to clinical therapy, one must remember that the absorption by the large intestine of the dog may not be comparable with that of the human being. However, it would seem that these findings should receive major consideration until such time as reliable information is available concerning absorption from the colon in man.

SUMMARY AND CONCLUSIONS

The practicability of the chronic closed colon loop for studying absorption has been demonstrated. Such disturbing factors as regurgitation, narcotization, visceral trauma, psychic disturbance, bacterial action and objectionable indications of absorption have been eliminated or reduced to a minimum.

It would seem that the optimum absorption of dextrose from the colon is from solutions between 5 and 10 per cent in strength, that the addition of small amounts of sodium chloride does not facilitate the absorption of dextrose and that sodium bicarbonate in the amounts used retards dextrose absorption. Dextrose is absorbed approximately one-half as fast by the transverse colon as by the lower ileum.

As regards water, it was noted in these experiments that the optimal solution for absorption is from a 0.9 per cent sodium chloride solution. Dextrose, in percentages as low as 2.5, inhibits water absorption and a definite water influx occurs when solutions containing 10 per cent or more are used. Small quantities of sodium bicarbonate added to an isotonic sugar solution result in a marked influx of fluid into the gut.

Our experiments indicate that the small intestine is more irritable than the colon and that absorption is more easily inhibited in the small bowel by disturbing factors.

The systemic blood sugar is not a true index of sugar absorption from the intestine when the amount absorbed is small.

The action of bacteria, found in the closed colon loop, is not significant when the absorption period does not exceed one hour.

If we can apply these results to clinical practice, two types of enemas may be indicated. A 0.9 per cent saline enema should combat dehydration most effectively; whereas, a dextrose solution of 5 to 10 per cent should allow for a maximum of dextrose absorption without loss of body fluids. Where dehydration is to be prevented the addition of dextrose or sodium bicarbonate in any amount is probably inadvisable.

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ABSTRACTS

SLAY, HARRY, AND GERSHON-COHEN, J.

Experimental Studies in Gastric Physiology in Man. A Study of Pyloric Control. The Roles of Acid and Alkali. S., G. and O., Vol. LVIII, No. 6, June, 1934, pp. 935-955.

The authors state that gastric motility may be considered to be the result of three components: gastric peristalsis, gastric tonus, and the state of the pylorus. They consider briefly the first two of those components, and present experimental data, which, after analysis, cause the third component to emerge as the most important factor in gastric emptying.

All studies were made on human subjects by means of roentgen examinations. Cases were selected to represent the entire range of gastric acid secretory response from achlorhydria to hyperchlorhydria. All psychic factors were eliminated; no drugs were used. The examinations were carried out during the evening hours. The subjects were allowed to eat the usual lunch at noon, and at 3 P. M. two slices of dry toast and a cup of tea without cream were ingested. Nothing more was taken until 8 P. M. when the studies were begun.

The mouth test meal consisted of 250 c.c. of luke-warm tap water containing two ounces of barium sulphate. The gastric emptying time for each subject was determined under standard conditions, and rechecked. Very little variation in the emptying time in the same individual under standard conditions was found. All test substances used were added to the water and barium meal. The emptying time for the water and barium meal established, new studies were made in which hydrochloric acid (0.09 to 0.53 per cent) or sodium bicarbonate (1 and 5 per cent) solutions were used. Observations and records were made during the first five minutes, and at intervals of 15, 30, 60, 90 and 120 minutes after ingestion, or at such time when complete emptying had occurred, or a constant residue had been obtained.

In another group of subjects the effect of the direct application of these substances to the duodenal mucosa was made. In these subjects gastric motility with duodenal intubation had been determined. No change in gastric motility attributable to the presence of the tube was found. The test agent was slowly instilled into the duodenum while simultaneously the water and barium meal was taken.

Summary of Experimental Data

Group I. Weak Acid (0.09 to 0.23 per cent taken by mouth).

A. In three subjects who showed normal gastric acidity this agent produced a short delay in gastric emptying in one, no change in the second, while in the third subject there was a slight acceleration in gastric motility.

B. In seven subjects with hyperacidity there was no change in five, one showed a slight delay, another a small increase.

C. Six subjects with achlorhydria showed a marked delay varying from 50 to 150 per cent.

Group II. Strong Acid (0.24 to 0.53 per cent) taken by mouth.

In this group a marked motor delay was found in all instances regardless of the Ewald secretory response. The hyperacidity group showed least relative delay.

Group III. Sodium Bicarbonate (1 per cent) taken by mouth.

A. Three subjects with normal gastric acidity showed a definite decrease in the time of gastric emptying.

B. Seven subjects with hyperacidity gave the same response as the normal subjects. but showed relatively a greater decrease.

C. Six subjects with achlorhydria showed no variation from their emptying time as determined with the water and barium alone.

Group IV. Sodium Bicarbonate (5 per cent) taken by mouth.

A. In three subjects with normal acidity there was no change in two, while in one there was a definite delay.

B. In seven subjects with hyperacidity six showed a decrease in emptying time while no change was noted in one.

C. In six subjects with achlorhydria a definite motor retardation was produced.

In every meal ingested by an achlorhydric there was an immediate filling of the duodenal cap, while in the normals and hyperchlorhydrics this was not always found. In the achlorhydric there is never any acid material in the duodenum to cause pyloric closure, while in the others there may be some acid material in the fasting stomach and duodenum causing the contraction of the pylorus. The reaction of the material on the duodenal mucosa, just distal to the cap, controls the state of the pylorus. In the achlorhydric there was an uninterrupted passage of the bland meal from the stomach, while the weak acid meal upon reaching the duodenum caused closure of the pylorus and marked delay in emptying. In those subjects with normal acidity or hyperacidity no such marked delay was found. The author suggests the possibility that the neutralizing mechanism in the stomach and duodenum of the achlorhydric may be less efficient than in the normal or the hyperchlorhydric.

The weak alkaline meal caused increased motility in the normals and hyperchlorhydrics by neutralizing the acid present, while in the achlorhydrics it caused no change. The 5 per cent sodium bicarbonate meal causes delay in gastric emptying in the achlorhydric by virtue of its hypertonicity, which initiates the duodeno-pyloric reflex.

One fact stands out clearly from these data: Without a consideration of the gastric secretory response of the experimental subject no logical or consistent interpretation of the results would be possible.

The Effect of Duodenal Instillations upon Gastric Emptying.

In achlorhydrics the instillation of 1 per cent sodium bicarbonate solution into the duodenum had no effect on gastric emptying, while in normals and hyperchlorhydrics it caused a more rapid emptying. In all cases the instillation of 5 per cent sodium bicarbonate solution caused considerable delay in gastric emptying.

The hydrochloric acid (0.12 per cent) instilled into the duodenum of an achlorhydric caused marked delay in gastric emptying. In hyperchlorhydrics the delay was only slight. In all groups there was very marked delay in gastric emptying when 0.25 per cent hydrochloric acid solution was instilled into the duodenum.

In the experience of the author gastric peristalsis is an unimportant factor in gastric emptying. In achlorhydrics the stomach was seen to empty readily without visible peristalsis, while in other cases very vigorous peristalsis failed to empty the stomach as long as pylorospasm lasted. Peristalsis is probably unrelated to pyloric opening.

If the gastric contents in passing over the duodenal mucosa do not set up the duodeno-pyloric reflex, gastric tonus is the most important factor in gastric emptying. It exerts a constant positive force which empties the stomach promptly if the pylorus is relaxed.

In conclusion, the authors emphasize that without due consideration of the individual gastric secretory response no proper evaluation of the experimental data could be made. They liken the stomach unto a dumb waiter ever ready to deliver through its door, the pylorus, anything reaching it. The duodenum they liken unto a selective connoisseur, who promptly closes the door if the stomach contents are not acceptable. The pylorus thus is a door but emphatically not an autonomous one.

An analysis of a large amount of pertinent literature, and a large bibliography are given.

Seven figures and eight tables accompany the article.

Nelson M. Percy.

MALTBY, ERNEST J.

The Digestion of Beef Proteins in the Human Stomach. Jour. of Clin. Invest., 13:193-207 (March), 1934.

In most previous studies of the digestibility of foods, workers have usually contented themselves with measurements of the emptying time of the stomach. However, in the present study the author followed the amount of digestion by determining at a given time after ingestion, the extent to which the protein had been hydrolyzed in the stomach into the various fractions.

Three types or classes of patient were used: (1) "normal" patients (those without gastro-intestinal disease), (2) achlorhydric individuals without pernicious anemia, and (3) achlorhydric individuals with pernicious anemia.

Following very complete and accurate and controlled determination, the author draws these conclusions: That considerable peptic hydrolysis of meat can occur in the stomach in a relatively short time; that there is a wide variation in the extent of this hydrolysis in the normal individual; that pernicious anemia patients accomplish little or no gastric digestion of meat; that achlorhydric cases without pernicious anemia have a small amount of gastric digestion; and that in his experiments the pepsin secretion and acid secretion appear to parallel each other in amounts.

As the author states, these conclusions are based on observations on a meat diet alone and may be different for a mixed dietary, yet this study may well serve as a start for further study of the function of the stomach in normal individuals and in those suffering from some gastro-intestinal pathology.

Elmer L. Eggleston.
George W. Slagel.

SECTION III—*Nutrition*

SOME OBSERVATIONS ON FOOD ALLERGY

By

WARREN T. VAUGHAN, M.D.*
RICHMOND, VIRGINIA

THE antiquity of "food idiosynerasy" is generally recognized. It is equally recognized that this is a manifestation of food allergy. And yet it is surprising how small a proportion of physicians realize what a relatively prominent part this plays in many disease complexes.

It has been shown that from seven to ten per cent of the population at large suffers from outspoken allergy such as asthma, hay fever, urticaria, allergic dermatitis, allergic migraine. We have found[1] that an additional fifty per cent have at one time or another suffered from some minor or evanescent allergic manifestation. Rowe,[2] Harkavy,[3] and Rackemann and Simon[4] find that from twenty-five to fifty per cent of the general population give positive skin reactions. The mechanism responsible for the allergic state is not so much a pathologic condition as it is a pathologic exaggeration of a normal physiological response. The mechanism usually considered necessary for the development of the allergic state exists normally in each of us. This has been shown by the work of Walzer and his associates.[5]

This latter work appears to me to be fundamental and will require some reconstruction of our understanding of the processes of protein digestion. It is still thought that protein is digested in the alimentary canal to its constituent amino acids which are absorbed as such, and certainly, that no incompletely digested protein passes into the systemic circulation beyond the liver barrier. The workers mentioned obtained serum from a case very strongly allergic to fish and injected it into the skin of a non-allergic recipient, thereby rendering this portion of the skin passively sensitized to the fish. This recipient then ate the fish in question and within a short time urticarial wheels appeared at the site of passive transfer. This was repeated, the work was checked with controls, and was produced again in a case sensitive to eggs. We must conclude, therefore, that egg and fish protein normally are absorbed into the systemic circulation and carried through the blood to the site of transfer, still sufficiently unchanged to be identified by this biologic reaction. Undoubtedly the protein was partially racemized but it is difficult to believe that it was entirely broken down into its constituent amino acids prior to arrival at the passively sensitized area.

In experimental animals we have become accustomed to feel that the one requisite for the production of the anaphylactic state is the introduction of foreign protein directly into the blood stream. If the work of Walzer and his associates is correct, and there seems no reason to doubt it, then the requisites for the production of the allergic state are normally present whenever protein foods are being assimilated. Why some persons do become sensitized under these conditions and why they manifest symptoms remains to be explained.

The surprising point is that, in the circumstances, more people do not develop allergic manifestations. As a matter of fact in our own amnestic survey of an entire community[1] we found that sixty per cent of the population had had either major allergy or minor allergic manifestations in the past and that the allergic inheritance was equally great in those who had suffered no allergy as in those that had. It, therefore, seems possible that one hundred per cent of the population would eventually develop some allergic symptoms if they were to live long enough and should happen to be exposed to a combination of those conditions particularly likely to predispose to the allergic state such as heavy exposure to an allergen, some intercurrent illness, etc.

Of course some persons develop allergy more easily than others. An outstanding factor in these cases appears to be the degree of inheritance.

Observations such as the foregoing, have led me to the conclusion, as stated, that allergy is not so much a pathologic state as it is a pathologic exaggeration of a normal physiological response.

Another conclusion which I have reached in my studies and which has a very important bearing on the problem at hand is, that the natural tendency in allergic sensitization is toward recovery, that is, toward loss of the specific sensitization. Allergic sensitization is usually temporary although it may last for years. This would explain in part why sixty per cent or more of the population finds it unnecessary to consult a physician for the relief of their allergic symptoms. There is another equally important reason which we will mention later.

Man may be sensitized relatively easily to horse serum. This is demonstrated in serum sickness. Frank or major allergics will, under observation, lose their sensitiveness to one food or other allergen and in the meantime develop a new sensitization. Serial testing over a period of years shows quite a variation in this respect. Although specific sensitization may last for years and in some instances undoubtedly for life, there are too many instances of recovery from sensitization after prolonged avoidance to negate the axiom which I have just stated, that the natural tendency is toward loss of sensitization.

This explains the unsatisfactory results of attempts at desensitzation to foods. Allergists have reached the conclusion that avoidance is better and enables the patient to return to eating that particular food sooner. I have seen a number of children who in infancy were extremely sensitive to eggs, both clinically and by test-

*Editor-in-Chief, Journal of Allergy.
Submitted July 20, 1934.

ing, and who through periods of five years or more had never touched eggs. Many of them had lost their sensitization completely. The question naturally rises, how long must one avoid an allergen to which one is sensitive, in order to lose the sensitization. It undoubtedly varies in different individuals. I have seen some patients who have avoided for twelve years and must continue to do so. Some appeared to lose their sensitization, or at least to return to a state of allergic balance or equilibrium in which they can tolerate contact with the offending foods, within so short a period as two or three months. In my experience with food allergy the average period of necessary avoidance is about four and a half years. If we could avoid all offending allergens for that length of time, on an average, we would lose our sensitizations. We are able to avoid pollens for eight or ten months but not for four and a half years. Therefore, we must be desensitized. But it is easier to avoid foods and, in this form of allergy, avoidance should be practiced.

The other factor which appeared responsible for the mildness and temporary character of symptoms in the fifty per cent in my experience manifesting minor allergy, was, to me, most interesting. By far the vast majority of persons in this group were able to name the substance responsible for their symptoms. And almost always these were substances with which the individual came into only occasional contact. The individual had no difficulty in recognizing the cause of his symptoms, because, with the foods for example, he had just eaten something which was unusual to his dietary. Thereafter he avoided that particular food, thereby curing himself. A minor allergic is a minor allergic because he becomes sensitive to something with which he establishes only occasional contact, he recognizes it as the cause, and avoids it. Students of allergy have for several years stressed the observation that an allergic individual usually becomes sensitive to something with which he comes into rather continuous contact. This is true of the major allergics or frank allergics but is not true of the minor allergics. The major food allergics become hypersensitive to wheat, egg, milk, potatoes, beans, etc., while the minor allergic reacts to onion, cabbage, cauliflower, cucumber, cantaloupe and the like.

Indeed, this appears to be the reason why some are major and others minor. I have also called them "fortunate" allergics and "unfortunate" allergics, because it appears to be in great measure merely a matter of luck as to what one becomes sensitized against. The unfortunate allergic, sensitive to wheat or some other daily constituent of his dietary, is unable to recognize the cause. He helps form the seven to ten per cent who must consult a physician and be studied allergically in order that the etiologic agent may be recognized.

In a pamphlet distributed by The Exhibit on Nutrition in the Scientific Exhibit of the meeting of The American Medical Association in Cleveland in June, 1934, the following statement was made: "The following foods in the order named were found most often to be the cause of digestive trouble: cabbage, apples, tomato, milk, chocolate, onion, lettuce, coffee, strawberries, eggs, meat, cucumber, sweets, fats, radishes, cheese, cauliflower, peppers, prunes, oranges and salmon. Food allergy is not considered in this list."

As a matter of fact that list comprises with few exceptions those foods to which in my own experience individuals are most often found to be allergic. It is indeed a list of food allergy. If one person develops urticaria or headaches or even just indigestion from the eating of cucumbers, while all of his friends have no unpleasant symptoms therefrom, he reacts differently from the others to cucumber. By definition he is a case of allergy to cucumber. It makes no difference whether the skin test be positive or not.

One need not have asthma, hay fever, migraine, eczema, urticaria or mucous colitis to be suffering from food allergy. There are many other manifestations, often quite obscure. Furthermore, food allergy may exaggerate the symptoms of other organic disease. Fifteen years ago it was thought that one of the diagnostic symptoms of gall bladder disease consisted in the patient being able to name certain specific foods as bringing on the typical attacks. The work of Auer[7] and of Valy Menkin,[8] showing that irritation and infection cause a mobilization of circulating antigens in the area so affected, give a physiological basis to our own observation that a person with true bile tract infection who is at the same time allergic to foods may precipitate a true gall bladder attack by the eating of allergenic foods; and to the observation of Kern[9] that peptic ulcer in persons allergic to milk heals much more rapidly if the ulcer diet contains no milk or milk products.

Allergy to foods is undoubtedly the commonest manifestation of clinical hypersensitiveness. It does not always manifest itself as one of the outspoken allergic diseases. The man who bears in mind this possibility and searches for the cause will often find gratifying success in many of the minor symptoms of obscure etiology, such as canker sores, recurrent herpes, chronic or recurrent headaches whether migrainous or not, and a long list of indefinite ill defined gastrointestinal complaints for which no other cause is found. One should also bear in mind that food allergy may complicate other organic pathology as mentioned above.

Methods of allergic study merit serious consideration. Too many appear to feel that the skin test is the court of last appeal and that, this being negative, allergy has been ruled out. This is but one of several methods of study, all of which must sometimes be brought into use for a successful solution of the patient's problem.

The deficiencies of the skin test method, particularly with respect to food allergy, are well known. This method certainly gives not over fifty per cent of the desired information. The writer's first attempt at improvement[10] on this was in the direction of a clearer understanding of the nature of the allergens themselves. With this in mind we established a logical grouping of the vegetable foods, based upon their biologic or genetic relationship. The previous culinary grouping into fruits, nuts, starchy vegetables, leafy vegetables, condiments, etc., was discarded.

We found that when biologically related food extracts were pooled and made into a single intracutaneous extract, the group extract was sometimes positive although the patient had been negative to the individual members of the group. In explanation we postulated a *synergistic effect*. The patient was then advised to watch all the members of the group and was sometimes able to discover the offending allergen in this way. Also, knowing the related foods we not infrequently find a positive reaction to one member of a group which fails to cause symptoms while another member reacting negatively is found to be responsible for trouble. In this way we were able to obviate some of the so-called "false negative" skin reactions. Biologically related groups are exemplified by the peach group which contains almond, peach, cherry, apricot, plum; the potato group which includes Irish potato, tomato, egg plant and red and green peppers; the mustard group, including mustard, radish, turnip, cabbage,

cauliflower, Brussels sprouts, broccoli, kale, kohlrabi; the cucumber group with cantaloupe, cucumber, melon, squashes, pumpkin, and the celery group, with celery, carrot, parsley, parsnip. This method requires a knowledge of the food groups[11] and further requires the intelligent co-operation of the patient in studying the effects of eating individual members of the suspected groups.

Rowe[2] next suggested further improvement in the elimination diet. This also was a result of efforts to find those offending foods which had failed to give positive skin reactions. In my own work, while I do not use Rowe's diet I do employ the same principle. Instead of at once placing the patient on serial standard diets[12] we first perform the sensitization tests, gaining thereby what information can be had therefrom, and then make up for each patient an individualized elimination diet or "trial diet" from which the foods to which he has given positive cutaneous reactions and their related "cousins" have been eliminated. By this method it is seldom necessary to go through a long series of diets, since the positive skin test foods have already been eliminated and need not be found by the method of trial and error. There is another disadvantage of the standard elimination diet.

I have said that the major allergic is sensitive to foods with which he comes in frequent contact while the minor allergic is sensitive to occasional foods. This must be modified in saying that we have found that the major or "unfortunate" allergic is at the same time sensitive to the occasional foods quite as frequently as is the minor allergic. Therefore, in his case we must search both for staples and for occasionals. The elimination diet is based in part on the assumption that foods eaten rarely are not likely to be allergenic. This in our experience is not the case even with major allergics.

The food diary, as we have developed it, is very simple to keep and read but sometimes difficult to analyze. However, it is often worth the effort since only by this method have we at times been able to discover offending foods which have failed to give positive cutaneous reactions. It is not of assistance when symptoms are constant since it is based upon the principle that foods eaten within twenty-four to thirty-six hours prior to an allergic outbreak may be responsible therefor. If the outbreaks occur not oftener than twice weekly one frequently has no difficulty in discovering some food or a few foods which are eaten just prior to the allergic episode. Rinkel has recently developed an improvement[13] on our own double form for the food diary, a "daily diet and symptom record" by which it is sometimes possible to find etiologic food agents even though symptoms occur daily. This he uses in conjunction with our own monthly diet record.

In our own studies we have from the first emphasized the desirability of attaching some significance to borderline positive skin reactions. Obviously when the degree of sensitization is unknown and when an allergenic food may even give a negative skin reaction, the borderline reaction may be of significance. At the same time it becomes evident that if the borderline reaction is considered in the same class with the positive reactions, there will be a large proportion of false positive reactions, since not every borderline reaction is really positive. However, we find it easier to start out with a strict diet in which all positive and borderline foods are eliminated, and then, with relief of symptoms, to add one food after another to the diet, thus finding those which are actually causing trouble. It is not enough just to eat a food once and decide whether it is causing trouble. *The action sometimes is cumulative.* To determine whether a suspected food is causing trouble it should be eaten two or three times daily for at least four days in succession, unless it has produced symptoms before the end of the test period.

With the procedure of skin testing, group testing, trial diet and food diary, as they are used in our own work, we find that for every two hundred positive skin tests to foods, one hundred are actually causing trouble. Half of them have been false positive. This is due in measure to our inclusion of the borderline reactions, but not entirely so, since one may give a strong four plus positive to a food that does not cause trouble. For every one hundred foods found actually to be causing trouble by the skin test method, forty additional foods are found by the method of the food diary. It becomes obvious that a combination of the methods gives best results.

In an attempt to still further improve our diagnostic methods with food allergens the writer has recently developed the leucopenic index method of study.[14] Several years ago Widal, Abrami and Iancovesco proposed the colloidoclastic or hemoclastic crisis test as a measure of liver function. This consisted in the giving of 200 c.c. of milk to the patient, in the post-absorptive state. A positive reaction, indicating liver damage, consisted among other things in a fall in the white count over a period of hours. While this was found not to be a reliable test of liver function the author observed that several individuals who did give positive hemoclastic crises were allergic to milk. Since the anaphylactic blood response is by leucopenia, it seemed possible that a digestion leucopenia following the ingestion of an allergenic food might turn out to be specific.

Following a study of over two hundred leucopenic index reactions, in over sixty patients and with a large variety of foods, the writer found that while the reaction is not constant, there is evidence that the ingestion of a food to which an individual is sensitive is followed by leucopenia. The leucopenic index method of study for food allergy is sixty-seven per cent reliable, a percentage as great as or greater than that of the skin test method. A disadvantage is that it is time-consuming and only one food may be tested at a time. In our experience, however, it has a definite place in that it may be used where some particular food is in question and with those foods which notoriously give false negative skin reactions. We have found the method to increase our diagnostic efficiency five per cent in the presence of false negative skin reactions and about the same amount in the presence of false positive skin reactions. A ten per cent enhancement of our diagnostic efficiency when added to the other methods of study is a distinct aid.

It has been said that *food dislikes* are a suggestive index to food allergy. My own experience is that the food to which an individual is allergic is more often that which he likes unusually well. In a careful analysis of six hundred cases, I was unable to find any correlation between food dislikes and food allergy.

DISCUSSION

In the foregoing, I have attempted to bring out the importance of food allergy in general medicine, particularly as applies to gastroenterology, and to emphasize the fact that the skin test is not the ultimate objective of the allergic diagnostic study but is just the beginning, and is, indeed, in many instances one of the less important features of the case analysis. Since, unfortunately, allergy to foods is as a rule multiple in the individual case; since the frank allergic is usually sensitive both to staples and to occasional foods; and since

in almost every case there are some etiologic foods which fail to react positively to the laboratory methods of study, the final analysis of the case often requires most painstaking effort and collaboration on the part of both doctor and patient and is often not reached until after months of painstaking study.

I have not mentioned one phase of the analysis because I wish to emphasize its importance at this point. This is what I term "discussion with the patient". It is not the mere routine history. The busy man in medicine is often too prone to take stereotyped history and proceed rather impatiently to the physical study and laboratory procedures. It is truly surprising what interesting things an individual allergic to foods can tell his doctor if given an opportunity. At the first discussion, which we might call "the routine history", not so much will develop. But when the initial studies have been completed and the patient is ready to be placed upon a preliminary program, and when he has gained some understanding of what we are endeavoring to accomplish, if one will sit down with him and discuss the positive and borderline reactions one will be surprised to discover that the patient, with this jog to his memory, will remember many curious and interesting incidents following the eating of foods, which he completely forgot to mention originally.

Discussion with the patient, as the case proceeds, often uncovers additional interesting episodes. This is the best way to discover curious and unusual low-grade allergic manifestations.

If one will take a presumed allergic case who does not seem to be getting along so well as he should, out to lunch, and, over coffee and cigars, chat unhurriedly for an hour or so, one will unearth much which is sometimes of intense interest.

These patients are usually of the chronic invalid class. Relief to such sufferers fully justifies the time and effort expended.

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REVISED "ELIMINATION DIETS" FOR THE DIAGNOSIS AND TREATMENT OF FOOD ALLERGY

By

ALBERT H. ROWE, M.D.
OAKLAND, CALIFORNIA

"ELIMINATION DIETS" were suggested first in 1927 and published in 1928[1] and again in 1931[1,6] for the diagnosis and treatment of those cases of food allergy not controlled by diets based on positive skin reactions to foods. This term "elimination diets" has been used by other writers since then to indicate diets composed of foods giving negative skin reactions in the patient. Such diets rather should be called "test negative diets" as suggested by Rockemann and the term "elimination diet" should be reserved for that type which the writer outlined—one which contains a minimum number of foods which infrequently produce allergy and foods to which the patient gives no definite skin reactions or history of idiosyncrasies. With such foods it is possible to formulate acceptable meals which meet metabolic and caloric requirements.

Those foods which infrequently produce allergy were chosen in 1928 after a careful study of 175 patients experiencing food sensitizations. Their clinical food allergies were indicated by positive skin reactions in approximately 50 per cent of such allergies. Most patients gave one or more suggestive or definite reactions to food allergens but not necessarily to any or all of those foods to which clinical allergy actually existed. This difficulty in demonstrating all food allergies by skin reactions was stressed by Alexander[2] and other investigators, which literature has been recently reviewed.[3] Vaughan[4] has concluded that two out of seven food sensitivities fail to give any skin reactions but in order to obtain that efficiency with skin testing he used the scratch followed by the intradermal method, retesting his patients and also taking the borderline and delayed reactions into account. He affirms[5] the importance of trial diets composed of a foundation list of foods to which he has found patients are infrequently sensitive together with other foods which skin reactions and the patient's history of food idiosyncrasies fail to indicate the presence of allergy. The writer's study since 1928[6] of several hundred patients with food allergy has confirmed the selection of foods which infrequently produce allergy and has continued to emphasize the negative skin reaction and the importance of trial diets modified by skin reactions and histories of food idiosyncrasies for its diagnosis.

Space does not permit a full discussion of the[6] frequency of food allergy as a cause of its various manifestations. Suffice it to say that in infancy and childhood, asthma, recurrent so-called head and bronchial colds, eczema, hives and gastro-intestinal disturbances, including cyclic vomiting are freqently due to food sensitizations. Tolerance for foods due to partial or at times complete desensitization gradually or occasionally spontaneously develops as the age increases

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and from the allergic viewpoint inhalant, contact, and to a lesser degree, bacterial allergies arise and assume importance. In the adolescent, adult and even the senile years, food allergy as a cause of many disturbances, severe, mild or often obscure in nature, is more frequent than formerly supposed. Because of the occurrence of negative skin reactions this can best be appreciated by the frequent and accurate use of diet trial. In adolescents and adults it is necessary to consider food allergy in the etiology of many cases of bronchial asthma, perennial hay fever, urticaria, angioneurotic edema, general toxaemia, unexplained fever, migraine and various gastro-intestinal disturbances. Certain ocular, urogenital and even cardiovascular symptoms at times arise from food sensitizations. The literature abounds with evidence for this frequency of food allergy throughout life and most contributions in the last few years suggest that "elimination diets" or other trial diets should be used when skin reactions to foods are negative or when diets based on skin tests fail to relieve the symptoms assumed to be due to food allergy.

Before listing the diets it is necessary to emphasize that this discussion of food allergy does not minimize the importance of inhalent and to a lesser extent bacterial allergy, alone or combined with food allergy, as the cause of many nasal, bronchial or cutaneous manifestations. Patients with cutaneous, nasal or bronchial disturbances which are so often due to inhalant allergies entirely, or associated with food or more rarely bacterial sensitizations should also be tested with all important inhalant allergens by both the scratch and intradermal methods, remembering that negative skin reactions also occur in approximately 10 per cent or more of inhalant sensitive individuals. Stevens[7] recently reports negative or slightly positive skin reactions in approximately 50 per cent of patients with pulmonary allergy to animal emanations. The proper control of inhalant allergy is at times necessary for satisfactory results from the exclusion of foods productive of concomitant allergy. It is to be stressed that careful and thorough physical examinations and laboratory studies must rule out all possible pathological causes for the various symptoms before food allergy is finally considered as the cause. Moreover the writer[4] has always recommended skin tests[1,6] by the scratch and later if desired by the intradermal method with those allergens which fail to react by the scratch test. However he agrees with Coca[8] that the scratch test will usually reveal those food allergies associated with skin sensitizing bodies. Such skin sensitizing bodies in infants may be absent in the presence of food allergy as emphasized by Smyth and Bain.[9] They state that such are rare in infants under four months regardless of sensitivity or contact with allergens. These skin test antibodies occur most frequently thereafter in the first years of childhood, gradually decreasing up to the teens and becoming less frequent as age increases. Recent studies[5] showed that selected patients, clinically sensitive to known foods to which scratch tests were negative, usually gave negative reactions by the intradermal method to such foods or gave indefinite or non-specific reactions to other foods to which the patient had no clinical allergies. The instability of certain food extracts was demonstrated. But food allergy cannot be ruled out in the absence of negative skin reactions or by the failure to obtain relief by "test negative diets" without the further use of trial diets which exclude foods commonly productive of allergy. For these reasons "elimination diets" have been devised. Even with such diets it is difficult to discover all food sensitizations in a few patients who are sensitive in mild degrees to a large number and variety of foods.

At this time certain changes are offered in the "elimination diets" which experience has shown will help physicians and patients. Menus have been arranged which allow various choices of foods and are easier to prescribe than those formerly outlined. A few changes have been made in the vegetables, fruits and miscellaneous foods in each of these diets. A cereal free diet is now offered as Diet 3. This was formerly included under the supplemental diets but in the last three years has been found of such value that it is now listed as one of the main "elimination diets". Vaughan[10] has emphasized the group sensitizations to foods and the writer has found many patients sensitive to cereals as a group as well as to one or more other foods. Diet 1 moreover excludes all pit fruits and legumes to take care of possible group sensitizations to such foods. Certain supplemental diets similar to those suggested in 1931[6] are again included.

THE DIAGNOSIS OF FOOD ALLERGY

When symptoms indicate the possibility of food allergy the following aids are available for the diagnosis:

(1) A positive personal or family history of allergy emphasizes the allergic tendency. However absence of such history does not conclusively rule out allergy in the patient. Few individuals fail to develop some sort of allergy during life as shown recently by Vaughan[11] who found that 60 per cent of 508 individuals in a small community had a past or present history indicative of allergy. The writer finds that the tendency to a specific kind of allergy, be it pollen, food, or animal emanation, is often inherited as well as the susceptibility to the actual manifestations such as asthma, migraine, eczema or gastro-intestinal symptoms. A careful history often suggests certain foods as possible causes of allergic manifestations. This fact has been stressed by the writer and recently by Vaughan who found histories of probable food idiosyncrasies in 62.9 per cent of his 508 average people.

(2) Skin testing with reliable clinically tested food allergens is indicated. Well executed and carefully interpreted scratch tests should be done first. The patient may then be tested intradermally with extracts of foods which have not reacted by the scratch method. Such intradermal tests have not yielded much additional information[3] of value in determining clinical food allergy. Marked reactions to foods frequently exist in the absence of clinical sensitizations to such foods, which fact emphasizes the necessity for the evaluation of all food reactions by diet trial. Diets based on skin reactions alone however frequently control symptoms.

(3) Patients who are not controlled by such "test negative diets" should be studied by further diet trial before ruling out food allergy. For this, "elimination diets" modified by positive skin reactions or histories of probable food idiosyncrasies are recommended, though other types of trial diet[6] as recommended by Brown, Alexander, Eyerman and Vaughan, may be used.

Though the information obtainable from skin tests is desirable in every patient, it is justifiable for physicians who are absolutely unable to test their patients because of expense or inability to refer them to allergists, to use the "elimination diets" modifying them by the patient's history of any food idiosyncrasies. The possible relief offered justifies such diet trial if skin testing is impossible.

USE OF ELIMINATION DIETS

When symptoms of probable food allergy are not controlled by diets which exclude foods to which skin reactions have occurred, or if skin reactions to foods are negative, or impossible to perform, "elimination diets" may be used. The frequency of the negative skin reaction to foods productive of clinical allergy and the occurrence of positive reactions to foods not causative of allergic symptoms must be remembered.

(1) Diets 1 and 2 first may be prescribed together or separately, modifying them by substituting similar foods for any in the diets to which skin reactions or known idosyncrasies exist.

(2) If sensitization to cereals as a group is suspected, Diet 3 may be used initially.

(3) Suggested menus for Diets 1 and 2 together and for Diets 1, 2, and 3 separately are detailed later. These menus indicate the ease of preparing meals which meet caloric and metabolic requirements with ries and a modified preparation of specified foods is foods in the "elimination diets". A reduction of calo- indicated for children according to age.

(4) The selected diet must be taken for at least ten days or even two to three weeks, for in many cases reacting bodies to the causative foods disappear very slowly from the shock tissues. If relief does not occur another "elimination diet" should be tried.

(5) Absolute adherence to the prescribed diet is imperative. Not the slightest bit of any food not specified must be taken. Restaurant and hotel food often contains slight amounts of forbidden foods, due at times to poorly cleansed cooking utensils or carelessness in cooking. No commercial breads, cookies, soups, etc., should be used unless every ingredient is known.

(6) If body weight decreases, specified sugars, starches and oils must be increased. Prescribed fruits and vegetables assure Vitamins A B, C and G. Adequate protein, when milk is excluded, requires meat or other protein two or three times a day. If milk is excluded longer than one month, the addition of 4 to 6 grams of dicalcium phosphate on retiring will assure mineral balance. Vitamin D must be supplemented by the use of cod liver oil, halibut oil, viosterol, sun or quartz light therapy. Until fish is added, fish oils cannot be used, and viosterol should be allowed only in an oil contained in the "elimination diets".

(7) With relief of symptoms longer than former periods of freedom, other foods, one to three at a time, from the remaining "elimination diets" are tried every four to seven days. Thereafter, other vegetables, fruits, meats, spices and nuts gradually may be added. In one to three months, milk, egg and wheat may be tried, separately, at fortnightly intervals. If the patient is allergic to any food, symptoms may occur immediately, or in days or even weeks according to the patient's tolerance. In such cases the food must again be eliminated.

(8) In the undernourished or in children, Diet 4 containing milk may be used first or milk may be tried, added to the chosen "elimination diet" in one or two weeks. Sobee, a soya bean product, or Cemac, containing beef and vegetables, are available for infants and children who cannot tolerate denaturized cow's or goat's milk.

(9) Desensitization by elimination may require weeks, months, or even years. With the above precautions, however, caloric and metabolic requirements are assured.

(10) The diagnosis, control and treatment of inhalant and contact allergies which may accompany food sensitizations are most important and not infrequently are necessary for satisfactory control of a food allergy.

SUPPLEMENTAL ELIMINATION DIETS

When Diets 1, 2 and 3 fail to relieve symptoms, then supplemental diets may be tried. Or they may be used initially if sensitizations to many different foods or to nearly all members of one or more groups of foods such as cereals, fruits, vegetables, or meats are indicated by history or skin reactions.

In the unsolved case of possible food allergy all foods must be suspected and minimal diets be selected as follows:

(1) A choice of one or two of the following carbohydrates: Rice, corn, tapioca, sago, sweet or white potato.

(2) A choice of one or two of the following protein rich foods: Lamb, beef, chicken, soya bean, lima bean, dried pea.

(3) A choice of one or two of the following vegetables: Spinach, carrot, beet, artichoke, asparagus, pea, tomato.

(4) A choice of one or two of the following fruits: Lemon, grapefruit, pear, peach, apricot, pineapple.

(5) Mazola (corn), Wesson (cottonseed), olive or sesame oil; white vinegar if lemon is excluded; salt, cane or beet sugar, glucose.

The choice of the supplemental diet depends on the patient's history of food idiosyncrasies or any positive skin reactions, if testing is available, and on the clinical reactions to foods evident from diet trial. Unless weight reduction is desired, these supplemental diets should be used only by patients who co-operate by eating sufficient calories of the specified foods to maintain weight. If sensitization to whole groups of foods such as cereals, meats, or fruits is suspected, such groups may be excluded, providing the prescribed diet meets metabolic and caloric requirements. If allergy to meats is suspected, the legumes may be used to furnish necessary protein if they are not productive of sensitizations. Menus can be formulated and these supplemented diets may be developed as already suggested for Diets 1, 2 and 3.

DESENSITIZATION TO FOODS

During childhood, desensitization to foods may gradually occur even though they are contained in the diet. Such a result may be more apparent than real, however, since one manifestation such as eczema, urticaria, asthma, or gastrointestinal symptoms may be replaced by another, or the food allergy may remain latent to reassert itself in later years. In childhood and especially in adult life, elimination of the allergenic food is the most effective means for desensitization. This may occur spontaneously in a few weeks after the elimination of such food, or may require months or years. Oral and hypodermic desensitization meets with varying results in different hands. Recently Freeman[13] has reported success with hypodermic therapy in certain food sensitive patients. Urbach[14] has also recommended specific prepeptans for the eradication of food allergies. In America, allergists[15] have yet to affirm the value of his suggestions.

CONCLUSIONS

"Elimination Diets" as aids in the diagnosis and treatment of food allergies again are described. Certain revisions, new menus and recipes have been detailed. Symptoms of suspected food allergy which are not relieved by "test negative" diets may be studied with this elimination method of diet trial. The diets should be modified by positive skin reactions obtained

by routine testing with food allergens and by histories of food disagreements. However, it is justifiable to use "elimination diets" modified only by the history of food idiosyncrasies without skin testing if such tests are absolutely unavailable to the physician or patient. Only with the use of diet trial preferably aided by skin reactions can the true frequency of food allergy throughout life be realized.

ELIMINATION DIETS (ROWE)

Diet 1	Diet 2	Diet 3	Diet 4
Rice Tapioca	Corn Rye	Tapioca White and Sweet Potato	Milk*
Rice Biscuit Rice Bread	Corn Pone Corn Rye Muffin Rye Bread Rye Crisp	Lima Bean Potato Bread Soya Bean Lima Bean Bread	
Lettuce Spinach Carrot Beet Artichoke	Tomato Squash Asparagus Peas String Beans	Beets Carrots Lima Beans String Beans Tomato	
Lamb	Chicken Bacon	Beef Bacon	
Lemon Grapefruit Pears	Pineapple Peaches Apricot Prunes	Lemon Grapefruit Peaches Apricot	
Cane Sugar Wesson Oil Olive Oil Salt Gelatin Syrup made of Maple Sugar or Cane Sugar or Cane Sugar Flavored with Mapleline or Maple Sugar Olives Pear Butter	Cane Sugar Mazola Oil Wesson Oil Salt Karo Corn Syrup Gelatin	Cane Sugar Olive Oil Wesson Oil Gelatin Salt Olives Maple Syrup or Syrup made with Cane Sugar flavored with Maple	

*Milk should be taken up to two or three quarts a day. Tapioca cooked with milk and milk sugar also may be taken.

Note: Wesson (Cottonseed) Oil is included in all diets. With allergy to cottonseed as shown by skin test or history this must be excluded and a cottonseed oil shortening such as Crisco must not be used. If allergy to cane sugar is suspected, beet sugar or corn glucose may be used.

DETAILED FOOD LISTS OF ELIMINATION DIETS (ROWE)

BREAKFAST

	Diets 1 and 2	Approximate Amounts
BEVERAGE	(a) Grapefruit (fresh) juice or lemonade with sugar as desired.	1 glassful
	(b) Pineapple juice.	
CEREAL	(a) Boiled brown or polished rice or cooked corn meal served with apricot, peach or prune juice and sugar.	½ cup rice 3 teaspoons juice or
	(b) Rice Crispies or Corn Flakes served with grapefruit juice and sugar or with apricot, peach or prune juice or maple syrup.	¾ cup dry flakes
	(c) Cold Rice or corn meal fried in Mazola oil or bacon or chicken fat served with maple syrup or Karo corn syrup.	
MEAT	(a) Bacon (mod. crisp) or	3 slices or
	(b) Lamb chops, Lamb or Chicken Croquettes (1)	1 med. chop
	(c) Lamb kidney fried with bacon	
BREAD	(a) Corn pone (2)	2 Muffins or 2 slices toasted
	(b) Corn Rice Muffin (3)	
	(c) Corn Rye Muffin (4)	
	(d) Rice Biscuit (5)	
	(e) Rice Bread (6)	
	(f) Rye Bread (7)	
	(g) Rye Crisp.	
JAMS OR PRESERVES	(a) Peach or Prune Jam	2 tablespoons
	(b) Apricot or Apricot Pineapple Jam or Preserves	
	(c) Grapefruit and Lemon Marmalade	
	(d) Pear Butter (9)	
FRUIT	Sliced or Whole Grapefruit, Canned, Fresh or Stewed Peaches, Apricots, Pears, Pineapple or Prunes.	

Notes: Choices as indicated by letters are offered in all menus though more than one may be used if desired. *Chicken meat and fat* should come only from broilers or roosters. Hens frequently have egg on them as a result of breaking unlaid eggs in dressing them. *Breads, Muffins and Cookies* should be made at home or by bakers who follow the recipes or similar ones as given in these diets. *Rye flour* especially is apt to be mixed with wheat and commercial rye bread practically always contains wheat and milk. *Corn Meal* can be obtained in different degrees of fineness.

This menu contains approximately—calories 612.

Gms. of carb.	92	Gms. of Ca	.104
Gms. of protein	15	Gms. of P	.200
Gms. of fat	20	Gms. of Fe	.0027

LUNCH AND DINNER

	Diets 1 and 2	Approximate amounts
SALAD	(a) Lettuce with apricot, peach, pear or pineapple with oil dressing or special mayonnaise.	2 halves or slices or
	(b) Vegetable salad made of tomato, carrots, beets, asparagus, peas, string beans or artichokes with oil dressing or special mayonnaise.	½ cup mixed vegetables 1 T oil or dressing
	(c) Sliced tomato or lettuce-tomato with oil dressing.	
	(d) Lemon gelatin with grated carrots and crushed pineapple.	
SOUP	(a) Lamb broth clear or with rice, carrot, peas, string beans as desired.	1 cup
	(b) Chicken broth clear or with rice, carrot, peas, string beans as desired.	
	(c) Split pea soup.	
MEAT	(a) Lamb served as chops, roast, tongue or stew made with lamb, rice, corn, carrots, peas, beets or string beans.	2 med. chops or
	(b) Chicken—roasted, fried, broiled, stewed. May be rubbed with bacon if desired or stuffed with rice or corn meal.	1 broiler or equivalent
	(c) Thicken gravy or sauces with rice flour or cornstarch.	
VEGETABLES	Spinach, carrot, squash, asparagus, peas, artichokes, beets, tomatoes.	4 T vegetables
BREAD	Choice of those in breakfast.	
JAMS OR PRESERVES	Choice of those in breakfast.	
DESSERT	(a) Fruit as suggested for breakfast	4 T fruit
	(b) Rice fruit pudding (10)	1 cup cake
	(c) Tapioca fruit pudding (11)	
	(d) Corn-rice cookie or rice cup cakes (12)	
BEVERAGE	(a) Grapefruit juice or lemonade with sugar. Corn dextrose may be used if extra carbohydrates is desired.	1 glassful

Notes: *It is best to use canned, preserved or fresh cooked fruits.* Uncooked fruits, other than grapefruit or lemon, are more apt to produce allergic reactions than heated fruits. Dried fruits well cooked with the exception of prunes are not well tolerated by certain patients. *Soups* may be made only with ingredients in the prescribed diets. Canned soups and those in restaurants and hotels are apt to have wheat, egg or other forbidden ingredients. *Meats* must not be cooked or basted with any food such as wheat flour, butter or spices not allowed. *Gravies* must be thickened only with prescribed flours. *Gelatin* may be incorporated in salads and desserts if desired.

This menu contains approximately—calories 864 *Total per day*—2340 cal.

Gms. of carb.	125	Gms. of Ca	.211
Gms. of protein	28	Gms. of P	.547
Gms. of fat	28	Gms. of Fe	.0091

BREAKFAST

	Diet 1	Approximate amounts
BEVERAGE	(a) Grapefruit juice or lemonade with sugar as desired.	1 glassful
	(b) Pear juice flavored with lemon	1 glassful
CEREAL	(a) Boiled or steamed brown or polished rice served with pear juice or maple syrup and sugar.	½ cup cooked rice 3 T syrup
	(b) Rice flakes or rice Krispies served with pears or pear juice and sugar.	¾ cup rice Krispies 4 T juice
	(c) Tapioca cooked in water and flavored with lemon juice, lemon rind and sugar.	1 T dry tapioca for one serving.
MEAT	Lamb chops or patties (13)	2 med. chops
BREAD	(a) Rice biscuits (5)	2 biscuits
	(b) Rice bread (6)	
JAM OR PRESERVES	(a) Pear butter (9)	2 tablespoonfuls
	(b) Lemon or grapefruit marmalade.	
FRUIT	(a) Sectioned or whole grapefruit	1 grapefruit
	(b) Fresh or canned pears	3 halves

Note. Corn sensitive patients often react to corn or glucose which must be excluded even in minute amounts.

This menu contains approximately—calories 768

Gms. of carb.	118	Gms. of Ca	.089
Gms. of protein	29	Gms. of P	.400
Gms. of fat	20	Gms. of Fe	.0046

LUNCH OR DINNER

	Diet 1	Approximate amounts
SALAD	(a) Hearts of lettuce. Dressing of olive or Wesson oil and white vinegar.	½ med. head 1 T oil
	(b) Vegetable salad of lettuce, carrots, beets, artichoke and olives as desired with above dressing or special mayonnaise.	1 cupful mixed veg.
	(c) Lettuce with sectioned grapefruit or pears served with oil and lemon juice dressing.	½ grapefruit or 2 halves of pears
SOUP	Lamb broth clear or with tapioca or rice and carrots as desired.	1 cupful
MEAT	(a) Lamb served as chops, roast, tongue.	2 med. lean chops
	(b) Stew made with lamb, rice or tapioca, carrots or beets. Thicken gravy with rice flour.	or their equivalent
VEGETABLE	Steamed or boiled rice, brown or polished.	½ cup cooked
	Spinach, carrots, beets or artichokes.	4 T
BREAD	Choice of those suggested for breakfast.	
JAM OR PRESERVES	Choice of those suggested for breakfast	
DESSERT	(a) Plain lemon or lime gelatin with pears or grapefruit as desired.	
	(b) Winter pears baked with maple syrup or brown sugar.	1 large pear
	(c) Rice cookie or cup cakes (12) (18)	1 cup cake
	(d) Puffed rice candy (14)	
	(e) Tapioca fruit pudding (11)	
	(f) Rice fruit pudding. (10)	
BEVERAGE	Choice of those suggested for breakfast.	1 glassful

Note: Pure olive oil and Wesson oil only can be used in Diet 1. Imported oil is usually adulterated. Wesson oil and Crisco must be excluded in presence of positive reactions to cottonseed.

This menu contains approximately—calories 914 *Total calories for day*—2596

Gms. of carb.	120	Gms. of Ca	.249
Gms. of protein	32	Gms. of P	.557
Gms. of fat	30	Gms. of Fe	.0109

BREAKFAST
Diet 2

			Approximate amounts
BEVERAGE	(a)	Pineapple or prune juice	1 glassful
	(b)	Apricot, peach and pineapple juices mixed	1 glassful
	(c)	Tomato juice	1 glassful
CEREAL	(a)	Corn flakes served with pineapple juice, or with peaches, apricots or prunes and juice and sugar.	4 T juice ¾ cup cornflakes ½ cup cooked cereal
	(b)	Corn meal mush served with maple or Karo syrup.	
	(c)	Cold corn meal mush fried in Mazola oil or bacon fat served with syrup and bacon.	
MEAT	(a)	Bacon	4 med. strips bacon
	(b)	Chicken croquettes (1)	1 croquette
BREAD	(a)	Corn pone (2)	2 muffins
	(b)	Corn and rye muffin (3)	1 or 2 slices toasted
	(c)	Rye bread (7)	2 Ry-krisp
	(d)	Ry-Krisp (8)	
JAM OR PRESERVES	(a)	Pineapple preserves	2 tablespoonsful
	(b)	Apricot or peach jam	
	(c)	Tomato cooked with sugar (15)	
FRUIT	Fresh, cooked or canned pineapple, peaches, apricots or prunes.		½ to ¾ cup

This menu contains approximately—calories 856.

Gms. of carb.	149	Gms. of Ca	.092
Gms. of protein	20	Gms. of P	.279
Gms. of fat	20	Gms. of Fe	.0042

LUNCH OR DINNER
Diet 2

			Approximate amounts
SALAD	(a)	Sliced tomato or asparagus with Mazola or Wesson oil and white vinegar or special mayonnaise.	1 large tomato and 6 to 8 stalks of asparagus
	(b)	Combination vegetable salad with tomatoes, asparagus, peas, and string beans as desired with above oil dressing.	2 T oil 1 cupful mixed veg.
	(c)	Combination fruit salad of pineapple, peaches and apricots with special mayonnaise thinned with pineapple juice.	1 cupful mixed fruits
	(d)	Chicken and pineapple salad mixed with special mayonnaise (16).	
SOUP	(a)	Chicken broth clear or with peas, string beans or tomato as desired.	1 cupful
	(b)	Split pea soup (17)	
MEAT	(a)	Chicken—roasted, fried, broiled, stewed. May be brushed with Mazola oil and rolled in corn meal if desired. Serve broiled peaches, apricots or pineapple with fried or broiled chicken.	½ broiler or fryer or its equivalent
	(b)	Chicken livers rolled in cornstarch or cornmeal and sautéed in Mazola or Wesson oil.	
	(c)	Thick slices of tomato fried or broiled in oil or bacon fat served with strips of bacon.	
VEGETABLES	Tomato, squash, asparagus, peas, string beans, corn.		4 tablespoons
BREAD	Choice of those suggested for breakfast.		
JAM OR PRESERVES	Choice of those suggested for breakfast.		
DESSERT	(a)	Fruits as suggested for breakfast.	4 tablespoons
	(b)	Rye cookies (18).	2 or 3 cookies
	(c)	Fruit cornstarch pudding with crushed pineapple. (19)	3 tablespoons
	(d)	Jellied prunes with pineapple. (20)	

This menu contains approximately—calories 1006 *Total calories for day*—2868

Gms. of carb.	118	Gms. of Ca	.138
Gms. of protein	30	Gms. of P	.522
Gms. of fat	46	Gms. of Fe	.0092

BREAKFAST
Diet 5

			Approximate amounts
BEVERAGE	(a)	Grapefruit juice of lemonade with sugar as desired.	1 glassful
	(b)	Tomato juice	1 glassful
CEREAL SUBSTITUTE	(a)	Tapioca cooked with apricot or peach, or flavored with lemon, maple sugar or caramelized sugar (20).	1 T dry tapioca ½ cupful
	(b)	Lima bean flakes served with apricot, peach, prune or grapefruit juice and sugar as desired.	¾ cupful l.b. flakes 4 T juice
MEAT	(a)	Bacon—moderately crisp.	4 slices
	(b)	Beefsteak, chipped beef, beef patties or tongue.	Small steak or its equivalent
	(b)	Bacon and hashed brown potatoes.	
BREAD	(a)	Lima bean-potato bread. (21)	2 slices toasted
	(b)	Lima bean-soya bean muffins. (22)	2 muffins
JAMS OR PRESERVES	(a)	Lemon or grapefruit marmalade.	2 tablespoons
	(b)	Peach or apricot jam.	
	(c)	Tomato preserves flavored with lemon.	
FRUIT	(a)	Sliced or whole grapefruit.	1 grapefruit
	(b)	Fresh, stewed or canned peaches or apricots.	4 tablespoons
	(c)	Sliced tomatoes with sugar.	

This menu contains approximately—calories 922.

Gms. of carb.	149	Gms. of Ca	.130
Gms. of protein	23	Gms. of P	.509
Gms. of fat	26	Gms. of Fe	.0078

LUNCH OR DINNER
Diet 5

			Approximate amounts
SALAD	(a)	Sliced tomato with olive or Wesson oil and lemon juice dressing or sugar.	1 large tomato 1 T oil
	(b)	Vegetable salad of carrots, lima beans, string beans, olives or tomatoes as desired with olive or Wesson oil dressing or special mayonnaise. (23)	1 cupful mixed vegetables
	(c)	Fruit salad made of grapefruit, peaches or apricot with above dressings.	½ to ¾ cupfuls of fruit.
SOUP	(a)	Beef bouillon clear or with carrots, lima beans or tomato.	1 cupful
	(b)	Lima bean soup flavored with bacon. (24)	
MEAT	(a)	Beefsteak, roast or tongue.	Average liberal serving of meat
	(b)	Beef stew with potato, carrots, lima beans or string beans. Thicken gravy with potato flour	
	(c)	Calves or beef liver and bacon.	
VEGETABLES	(a)	White or sweet potatoes.	1 med. sized potato
	(b)	Carrots, lima beans, string beans, tomatoes.	4 T
BREAD	Choice of those suggested for breakfast.		
JAMS OR PRESERVES	Choice of those suggested for breakfast.		
DESSERT	(a)	Fruits as suggested for breakfast.	4 T
	(b)	Tapioca fruit pudding. (1)	
	(c)	Lima bean-potato flour cookies or cup cakes frosted with sugar and lemon juice icing. (25)	2 cookies or 1 cup cake
BEVERAGE	(a)	Grapefruit juice of lemonade with sugar as desired.	1 glassful
	(b)	Tomato juice.	

This menu contains approximately—calories 901 *Total calories for day*—2724

Gms. of carb.	140	Gms. of Ca	.326
Gms. of protein	38	Gms. of P	.059
Gms. of fat	21	Gms. of Fe	.0190

RECIPES

(1) CHICKEN CROQUETTES

1 tablespoon oil or chicken fat
2 tablespoons cornstarch
½ cup liquid (chicken broth)
¾ cup cooked minced chicken
salt

Make a sauce of fat, cornstarch and liquid. Add the other ingredients. (Cooked cornmeal may be added.) Cool, shape, dip in rye flour or crushed corn flakes. Bake in medium oven or fry in deep fat.

(2) CORN PONE

1 cup cornmeal
½ teaspoon salt
Boiling water
1 tablespoon Mazola oil

Carefully pour enough boiling water onto the cornmeal to make a stiff mixture, stirring constantly. Add the oil and mix well. Mold into oblong "pones" and fry in hot skillet with enough fat to prevent sticking. When brown on one side, turn and brown on the other side. Serve hot.

(3) CORN AND RICE MUFFINS

½ cup rice flour
½ cup yellow cornmeal
2 tablespoons sugar
2½ teaspoons baking powder
3 tablespoons Mazola oil
½ cup water

Mix all the dry ingredients well, sifting them together four or five times. Add the water and oil. Bake in a hot oven twenty minutes.
Makes six small muffins.

(4) CORN AND RYE MUFFINS

Use the above recipe but substitute rye flour for rice flour.

(5) RICE BISCUITS

Made by the Battle Creek Sanitarium.

(6) RICE BREAD

1 cup rice flour
3 teaspoons baking powder
2 tablespoons bacon fat or oil
1 tablespoon sugar
½ teaspoon salt
¾ cup water

Sift the dry ingredients. Add water and fat. Bake in a loaf pan in a moderate oven.

*Fat used in recipes for greasing pans or shortening must only be oil or fat specified in the prescribed diet. Baking powder should be Royal or Schillings which contain no egg.

(7) RYE-RICE BREAD

½ cup rye flour
½ cup rice flour
½ teaspoon salt
6 teaspoons sugar
5 teaspoons baking powder
2 teaspoons olive oil
1½ cups water

Sift all the dry ingredients together. Add water and oil. Bake in a loaf pan in a moderate oven for forty minutes.

(8) RY-KRISP

Prepared by the Ralston Purina Company.

(9) PEAR BUTTER

Select firm, ripe pears. Peel, core and cut into rather small pieces. To two cups of prepared fruit add one cup of sugar. Cook slowly, stirring frequently to prevent burning, for two hours or until the mixture is quite thick.

(10) RICE-FRUIT PUDDING

Sauce:
1 cup sugar
2 tablespoons rice flour
½ teaspoon salt
1¼ cups boiling water
1 teaspoon lemon juice or vanilla

Mix sugar, salt and cornstarch. Add water and cook until thick. Remove from stove and add flavoring. Add boiled rice and apricots or sliced peaches and serve warm. Reserve some sauce to pour over the pudding.

(11) TAPIOCA-FRUIT PUDDING

2 halves peaches sliced
1 tablespoon dry tapioca
2 teaspoons sugar
½ cup peach juice and water

Drain peaches and sprinkle with one teaspoon sugar. Cook tapioca in juice and water until it is clear. Add remaining sugar and salt. Line a baking dish with peaches. Fill with tapioca and bake in a moderate oven twenty minutes.

(12) RICE CUP CAKES

¾ cup hot water
1½ cups rice flour
2 level tablespoons shortening
½ cup sugar
½ teaspoon salt
3 level tablespoons baking powder
1 teaspoon vanilla

Pour hot water over half the flour. Cream sugar and shortening and add to the above mixture, beating well. Add the other ingredients, mixing well. Bake in muffin pans about twenty minutes in a fairly hot oven.

(13) LAMB PATTIES

Ground lamb pressed into small patties. Broiled or fried.

(14) PUFFED RICE CANDY

1 cup sugar
½ cup brown sugar
1 cup water
¼ teaspoon salt
1 teaspoon vanilla
Puffed rice

Cook sugar, syrup and water until brittle. Add vanilla and salt. Pour puffed rice, stirring all the time so that the kernels will be evenly coated. Turn it into a greased pan and cut in squares. Keeps well in an air-tight container.

(15) TOMATOES COOKED WITH SUGAR

Select firm, ripe tomatoes. Remove the skins, cut in slices and drain an hour or more. For each cup of tomatoes add a cup of sugar and boil until thick, stirring often. Sliced lemon may be added to the tomatoes while cooking.

(16) CHICKEN AND PINEAPPLE SALAD

Cut cold boiled chicken into cubes and marinate for two hours in French dressing of oil and white vinegar and salt. Drain well, mix chicken with about ½ its volume of diced pineapple and add special mayonnaise, thinned with pineapple juice to taste.

(17) SPLIT PEA SOUP

1 cup green split peas
3 cups water
1 tablespoon bacon fat
Diced bacon (crisp)
Salt

Cook the peas until they form a smooth puree. Just before serving add salt, bacon fat and crisply fried bacon.

(18) RYE OR RICE COOKIES

1 cup rye or rice flour
¼ cup light molasses (or syrup)
3 tablespoons Wesson oil
½ teaspoon salt
½ teaspoon soda
1½ teaspoons baking powder
1 tablespoon sugar
Water to make a stiff dough

Mix dry ingredients. Add syrup, oil and water. Drop on a greased cookie sheet and bake at 325° for fifteen minutes.

(19) FRUIT CORNSTARCH PUDDING

1½ cups fruit pulp
1½ cups water
2 teaspoons sugar
5 level teaspoons cornstarch

Cook for ½ hour in the top part of a double boiler.

(20) TAPIOCA WITH APRICOTS

6 halves apricots, pureed
2 teaspoons sugar
1 tablespoon dry tapioca
½ cup juice and water.

Cook the liquid and tapioca in a double boiler until tapioca is clear. Add apricots and blend well. Serve warm with apricot juice.

(21) LIMA BEAN-POTATO MUFFINS OR BREAD

¾ cup potato flour
½ cup lima bean flour
3 teaspoons baking powder
½ teaspoon salt
4 teaspoons sugar
½ cup water
2 tablespoons shortening

Sift dry ingredients together. Melt fat and add to water, add slowly to dry ingredients. Put in greased muffin tins and bake at 400° F. for 20 minutes. Serve hot. Makes 10 small muffins.

(22) LIMA BEAN-SOYA BEAN BREAD

Substitute soya bean flour for potato flour in recipe for potato-lima bean bread.

(23) BOILED MAYONNAISE

1 teaspoon sugar
½ teaspoon salt
3 level teaspoons starch*
Juice 1 large lemon
½ cup boiling water
½ cup Mazola oil

Mix sugar, salt, starch and lemon juice. Add water, cook until thick. Remove from stove and slowly add oil, beating vigorously.

*Use rice flour in Diet 1, cornstarch in Diet 2 and potato flour in Diet 3.

(24) PUREE OF LIMA BEAN SOUP

Wash and soak for a few hours two cups of lima beans. Cook in plenty of water salted to taste. When beans are well done, put thru a sieve.

Cook small pieces of bacon, crisp. Add enough bacon dripping and crisp fried bacon to puree to make palatable.

(25) LIMA BEAN-POTATO CAKE AND COOKIES

6 tablespoons lima bean flour
¾ cup potato flour
5 tablespoons shortening
½ cup water
½ cup sugar
2½ teaspoons baking powder.
½ teaspoon vanilla
½ teaspoon lemon extract
Few grains salt, few drops yellow coloring.

Sift dry ingredients, cream fat and sugar, add dry ingredients and water alternately to creamed mixture. Add flavorings and coloring. Put in greased muffin tins and bake in oven at 430° for 30 minutes.

(26) BROILED FRUIT

Remove skins from ripe fruit (peaches, apricots, etc.). Cut in half and remove stone. Brush well with olive oil and sprinkle with sugar. Cook under a broiler until delicately browned, turning once. Garnish with chopped mint. Serve with broiled chops or chicken.

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ABSTRACTS

STRAUSS, M. B.

The Role of the Gastro-intestinal Tract in Conditioning Deficiency Disease. The Significance of Digestion and Absorption in Pernicious Anemia, Pellagra and "Alcoholic" and Other Forms of Polyneuritis. J. A. M. A., 103:1, July, 7, 1934.

The concept reviewed in this paper is that deficiency disease in man may and frequently does develop because of some disturbance in the gastro-intestinal tract in spite of an apparently adequate diet. In discussing pernicious anemia the author concludes that the disease may result from any one of three mechanisms or from any combination of them: (1) the lack of a digestive juice in the stomach, (2) the absence of a substance associated with vitamin B2 (G) from the diet, or (3) the failure of absorption from the intestinal tract of the product of interaction of the stomach and dietary factors. Pellagra, as commonly seen in endemic form, probably is due essentially to the lack of vitamin B2 (G) in the diet. In like manner, it is pointed out that gastro-intestinal disturbances practically always condition the development of multiple neuritides (beri-beri) in those regions where it is not endemic.

Samuel Morrison.

WAN, SHANG.

The Acidity of Gastro-Intestinal Contents of Vegetarian and Omnivorous Rats. (Chinese J. Physiol., 7, 179-184.) 1933.

Rats fed on a vegetarian diet were smaller than rats on a mixed diet. The calcium intake of the two groups was the same. Since the absorption of calcium is influenced by the pH of the intestinal contents, the pH of the gastro-intestinal tracts was determined in both groups to ascertain whether the differences in size were due to differences in the absorption of calcium. No significant differences were found. The chief value of the paper lies in the estimations of the pH of various portions of the gastro-intestinal tract.

M. H. Friedman.

SECTION V—*Therapeutics*

THE MANAGEMENT OF CHRONIC SPASTIC CONSTIPATION*

By

HARVEY G. BECK

BALTIMORE, MARYLAND

TWENTY-THREE centuries ago Hippocrates wrote in his aphorisms: "Persons in good health quickly lose their strength by taking purgative medicines or using bad food." He directed attention to the stimulating effect of whole meal bread as a laxative food. "Physic is not always good for the sick but is always hurtful to the healthy." Thus spake Celsius, who advocated drinking large amounts of hot water as a laxative.

Cicero's friend and physician, Asclepiades, was averse to the employment of violent remedies and especially condemned the excessive use of purgatives and enemas so much favored by his fellow practitioners. He advocated the use of music as a soothing agent and resorted to frequent bathing and massage.

In the sixth century, Alexander of Tralles also entered protest against violent purgation and recommended that treatment be deferred until a diagnosis was made.

Despite these wise counsels the abuse of purgation persisted, for in the year 931 A. D., when medical licensure originated at Bagdad, it is recorded that the first medical examiner, Sinan ibu Thabet, granted a license to an applicant on condition that he would not prescribe phlebotomy or any purgative drugs except for simple ailments.

Francis Bacon recognized the abuse and proposed dietary regulations as a substitute for purgatives.

Recounting these few facts culled from the literature of the ancients, it is obvious that the subject of constipation does not present any problems which are new and have not been fraught with considerable misgiving and often complete failure during these many centuries. It will be observed that the pioneers in this field especially emphasized the abuse of enemas and strong purgatives; the importance of suitable diets and plenty fluids; the value of physiotherapy (massage); hydrotherapy (baths) and psychotherapy (music); the necessity of a correct diagnosis, and the legal restrictions of physicians to prescribe purgative drugs promiscuously. It is difficult to conceive today even in the light of our present knowledge of a more ideal or rational therapy for constipation than one in which all of these ancient measures are properly combined and rigidly enforced.

It has been authoritatively stated that constipation as a symptom is the most prevalent to which mankind is subject. As a *disease*, which implies all of the underlying conditions with which it may become associated, it is said to be the most insidious and most deadly, destroying the health and happiness of millions while at the same time it is one of the most preventable diseases and one most easily cured by simple methods if intelligently applied at the proper time. However, should prevention be utterly disregarded and either no attempt be made at cure, or what is worse, recourse be had to some of the many fraudulent remedies so extensively exploited through the press and over the radio, the ultimate outcome is the development of a form of chronic invalidism from which many sufferers never recover. This is the result largely of underestimating the significance of the symptoms, and mismanagement or inadequate and unscientific treatment.

The objects in presenting this paper are *first* to make an appeal for a more concerted effort on the part of the profession to counteract the evil influences of misinformation and ruthless distortion of facts, methods used in the commercial exploitation of pseudo-scientific and fraudulent remedies solely for financial gain; and *second*, to stress the importance of a more thorough and scientific application of knowledge in the treatment of constipation in order to relieve the miserable sufferers who have become the victims of fraud, neglect or injudicious treatment. As Welch has stated, it is not so much that we need more knowledge but a more universal application of that we already possess.

The frequency with which sufferers of constipation seek relief from their symptoms may be inferred by the fact that out of 7,000 consecutive cases studied in a private clinic 430 were either partially or wholly invalidated as the result of this malady. In most of the patients the constipation was of the spastic variety and many were in an advanced stage in which they were subject to a variety of complications such as colitis, gastroenteroptosis, coloptosis, adhesions, stasis, dilation and kinking of the colon, in addition to constitutional disturbances such as malnutrition, anemia and certain psychic and nervous manifestations of a toxic and reflex nature which form a clinical syndrome to which the Germans originally applied the name "enterics".

A knowledge concerning the various causes and clinical forms of constipation is essential to successful treatment. The general causes may be divided into

(a) *Constitutional*—bradymorphic or megalosplanchnic type with redundant colon.

(b) *Habits*—of the sedentary type in individuals who eat too much and exercise too little.

(c) *Diet*—which fails to produce sufficient residue or is so irritating that it causes colonic spasm.

(d) *Diseases*—secondary to affections of the liver, stomach and intestines, anemia, functional neuroses and many others.

(e) *Drugs*—Osler stated that the most injurious of all habits is drug taking. Purgative medicines which act by irritating the intestinal mucous membranes

*From the Diagnostic Clinic, Baltimore, Maryland.
Read before the Annual Session of the American Therapeutic Society, Cleveland, Ohio, Jan. 9-10, 1934.
Submitted July 20, 1934.

never cure but perpetuate and complicate the disease by causing a spastic colitis.

(f) *Neglect* to respond when the normal impulse to defacate arises is one of the most common causes. Repeated neglect tends to lessen the sensibility, thus requiring a stronger stimulus, which results in atony and dilatation of the rectum, a condition for which Hurst introduced the word "dyschesia".

Among the *local* causes may be mentioned weakness and relaxation of the abdominal muscles due to overdistension from obesity or frequent pregnancies; tumors pressing on the bowels; foreign bodies and strictures; ptoses, adhesions and kinking of the colon; atony and dilatation of the colon; spastic contraction occurring in nervous vagatonic individuals or secondary to ulcerative colitis, etc.

Chronic constipation in its course of development passes usually through the three following stages:



Fig. 1. Shows condition of colon and duodenum before treatment.



Fig. 2. Note the improvement as a result of treatment six months later.

atonic, catarrhal and spastic. If it is not corrected in the last stage, it may lead further into a condition of membraneous enteritis, mucous colic, and stercoral diarrhea.

It has become customary to group constipation into the *atonic, catarrhal* and *spastic* forms. These three forms actually represent three consecutive stages in the course of development of chronic constipation and can readily be differentiated by few subjective symptoms and objective findings.

In the *atonic stage* patients do not complain of either pain or flatulence. Stools are normal in form and consistency and are of large calibre.

The *catarrhal stage* is recognized, subjectively, by the presence of flatulence, especially after gas-producing foods, but is not associated with pain. Objectively, the characteristic feature of the stool is the presence of membraneous mucus enveloping the scybalae.

The *spastic stage* is characterized by pain and flatulence, the pain being due either to flatulent colic or to mucous colic, and aggravated by purgatives, enemas or coarse foods. Objectively, the sigmoid can be palpated as a hard cord and is painful. On rectal examination, the sphincters are spastic and the rectum is usually entirely empty and contracted or it may contain small, hard fecal masses. Stool is small in calibre, often knotted and contains either free mucus which is occasionally blood streaked, or mucus mixed with dry, hard feces.

TREATMENT

As previously stated, in order to institute rational therapy it is necessary to have a thorough knowledge of the case to be treated which includes a clear understanding of the etiological factors as well as the stage of the disease from which the patient is suffering.

Atonic Constipation: Individuals suffering with this form are practically without symptoms and the constipation is relieved by any simple laxative drug or enema. The patients rarely apply for medical treatment. It is this stage which usually is neglected and almost certainly leads to the more severe catarrhal and spastic forms for which the physician is consulted.

The treatment of atonic constipation which is largely prophylactic against the more severe chronic spastic form, should be established upon a sound hygienic and dietetic basis. The patient should lead a normal life, develop regular habits in regard to exercise and meals, and should be enjoined to go to the toilet regularly every morning after breakfast. He should be encouraged to take plenty of exercise in the form of gymnastics, swimming, golf, horseback riding, etc. Enteroptotic patients should wear a suitable abdominal support. The diet should be calculated to furnish an abundance of residue. Accordingly, it should be rich

in cellulose which mechanically stimulates peristalsis. If a patient is undernourished, a high caloric diet is indicated. Drugs should only be used for temporary relief. Occasionally salines or some of the milder common remedies, such as rhubarb, senna or cascara may be resorted to.

"Catarrhal" Constipation: If the habit of self-medication develops, as is so frequently the case, even these milder purgatives may lead to the second stage of the disease; namely, the catarrhal form. However, this may not happen for many years. When the catarrhal stage is reached, if proper diet is not prescribed and purgative drugs countermanded, the condition will pass over in a comparatively short period into the more chronic and persistent form of *spastic constipation.* As the treatment of the catarrhal and spastic forms is essentially the same, they will be considered together. It is the long-standing spastic form with



Fig. 3. Female, aged 22. History of two "nervous breakdowns". Complained of headache, indigestion, vomiting, constipation, weakness, subnutrition and emotional and nervous instability. A diagnosis was made of gastric myasthenia, constipation with colonic stasis and spastic colitis in a neuropathic individual.

its many complications and sequelae that often taxes the skill of the alert physician and commands all the resources available in order to effect a permanent cure. The principles involved in the management and treatment of these types of cases can best be illustrated by citing a case now under observation.

Case Report: Patient, female, married, age 50, suffered with constipation for twenty-five years. In recent years, she was subject to periodic attacks of nausea, vomiting and pain in right side of abdomen. During the entire period of her illness she was in the habit of taking strong purgatives, some of them containing phenolphthalein. She personally attributed the acute attacks of nausea, vomiting and pains to the abuse of purgatives. As the condition progressed, she lost weight and strength and developed psychoneurotic symptoms. These included sleeplessness, irritability, lack of emotional inhibition, fears, doubts, obsessions and periods of profound depression.

Physical Examination: Patient presented the general appearance of one nervous, weak, anaemic and undernourished. She was twenty-two pounds under ideal, calculated weight and her blood pressure was 100 systolic and 56 diastolic. Heart and lungs were normal. The abdominal wall was thin and relaxed. There was an area of diffuse tenderness in the right iliac fossa where splashing sounds could easily be elicited by palpation or by gently rolling the patient from side to side. There were no palpable masses. The liver, spleen and kidneys were negative.

Laboratory Findings: Gastric contents after the Ewald test meal showed free HCl 27, total acidity 34

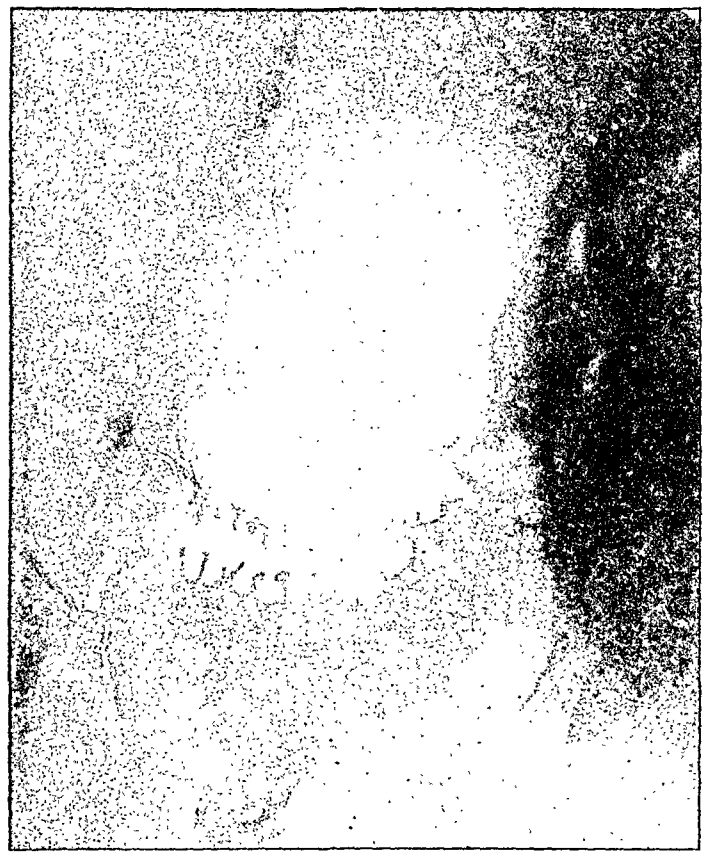


Fig. 4. The effect of two months' treatment based on the principles outlined.

and a considerable amount of mucus. Stool was normal in color, soft in consistency, admixed with mucus and was negative for occult blood and parasites. Blood examination showed hemaglobin 74, red cell count 4,180,000 and a normal white and differential count. All other laboratory studies were negative.

Roentgenologic Examination: Fluoroscopy in the erect posture revealed a normal stomach, moderately ptosed, displaced to the left on account of an enormously distended caecum and ascending colon which were divided into two portions: the lower containing barium and free fluid and the upper, above the fluid level, entirely occupied by a large accumulation of gas. Splashing of the fluid could be seen as well as heard on manipulation. Roentgenograms confirmed these observations. The caecum measured three and one-quarter inches in diameter; the first portion of the

duodenum was dilated and there was evidence of right upper quadrant adhesions. (Fig. I.)

A *diagnosis* was made of chronic, spastic constipation, chronic colitis, colonic stasis with dilatation and duodenal dilatation in a markedly psychoneurotic individual.

As the patient had reached the stage of complete invalidism and failed to respond to the usual method of treatment, a thoroughly organized and systematized rest cure was instituted. This comprised a period of rest in bed; well balanced, nutritious, non-irritating, laxative diet; warm, moist abdominal compresses; antispasmodics; hyponotics; mineral oil; dilatation of anal sphincters; physiotherapy and psychotherapy. The response to this plan of treatment was prompt and satisfactory. The nervous symptoms subsided, bowels moved daily with the aid of mineral oil and agar, the character of the stools returned to normal

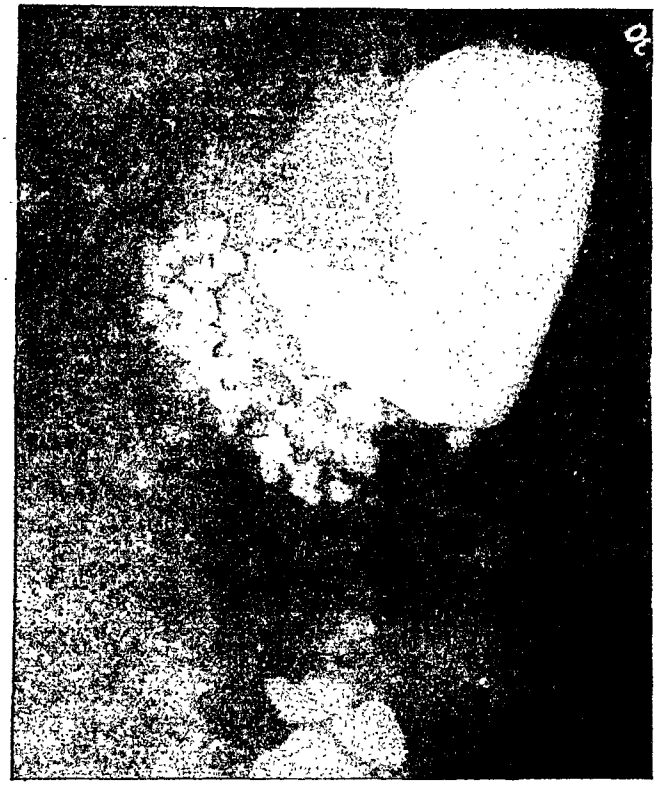


Fig. 5. Female, aged 33. Complained of abdominal pain, vomiting, constipation, headache, nervousness and loss of weight. Examination showed that these symptoms were associated with achylia gastrica, gastroenteroptosis, chronic spastic constipation, anemia and malnutrition.

and she gained in weight and strength so that she was able to return to her former household duties.

The dilatation, stasis and spasticity of the colon were almost completely restored to normal. (Fig. 2.)

During the period when patients are under a strict rest regime and treatment is conducted orderly and systematically under skillfully trained nurses, the physician does not need to be seriously concerned about their welfare. It is an entirely different problem, however, at the end of a rest cure when they return to their former environments and assume the responsibilities of the home in addition to the treatment.

This is the most critical period during the patient's convalescence. Success or failure depends upon whether or not the further course is pursued with diligent care and attention to essential details so that intelligent co-operation between the doctor and the patient is possible. It is unreasonable to suppose that one timid and weak from prolonged rest in bed is apt to remember every detail of instruction essential for cure if verbally rendered. Such advice is not only as a rule futile, but is often harmful, causing doubt and confusion which lead to despair and ultimate abandonment of treatment and hence complete failure.

Many failures of this kind induced me years ago to adopt the method of providing these patients with typewritten instructions in a simple, practical and concise form. In these instructions the diagnosis and results of previous treatments are set forth. In addition detailed instructions are outlined with respect to 1, Rest; 2, Diet; 3, Bath; 4, Compresses; 5, Abdominal Support; 6, Exercise; 7, Diversion; 8, Literature; 9, Medication; 10, Weight; 11, Reports, etc.



Fig. 6. Film taken six months later illustrates the effects of treatment. There was a corresponding improvement in her general health.

In the preface to these instructions, attention is called to the diagnoses and the patient is reminded of the manner and extent of improvement. This aids tremendously in conquering fears and doubts which are the arch enemies with which the physician has to contend in successfully curing any chronic disease in an invalid with psychoneurotic background.

One of the most effectual therapeutic measures in restoring the physical strength and emotional poise of the average woman during convalescence is a daily rest of an hour or two in bed at noon. As many functional nervous symptoms are the result of fatigue and as states of exhaustion interfere with both the secretory and motor functions of the stomach and intestines, it is desirable to prevent a fatigue syndrome by the simple prophylactic measure of such a period of rest daily.

Proper diet constitutes the most important factor in the treatment of spastic constipation. It is surprising the number of individuals who eat an imbalanced and inadequate diet. One can be readily convinced of this fact by making specific inquiry into the articles of diet the patient consumed during the meals of a single day.

The following list, introduced by Dr. Frank Smithies, serves all the requirements of an ideal diet for this class of patients:

BREAKFAST:	Eight stewed prunes, one sweet grapefruit, or five figs. Well cooked cream of wheat or oatmeal, or shredded wheat biscuit (use cream). Soft boiled eggs, or poached eggs. Graham or rye bread, with little butter. Two cups of hot water or very weak coffee.
AT NOON:	Creamed or strained soup, or soup from peas, beans, potatoes, celery, barley or vermicelli. Meat, very sparingly—every day may take not more than four ounces of rare beef, lamb chops, or white meat of chicken. Eggs, soft boiled or poached. Graham or rye bread, with little butter. Eat an excess of vegetables—spinach, asparagus, tender celery, tender string beans, cauliflower, mashed squash, mashed carrots. Eat an excess of prunes, figs, dates, apple-sauce, steamed peaches or apricots. Drink hot water, or milk and hot water, or hot water flavored with coffee.
AT NIGHT:	Similar meal to noon, except soup. In addition may choose broiled mutton, beef, bass, white fish, custards, gelatine, blanc mange, prune whip, tapioca, sage.
DO NOT EAT:	Strong tea, cocoa, chocolate, rice, blackberries, huckleberries, cheese, alcoholic stimulants.
GENERAL DIRECTIONS:	Eat very slowly, and chew thoroughly. Take nothing very hot or very cold. Forget worries at meals. Go to stool, once daily, in the morning, and stay for 10 minutes. Never eat until you are overfilled. Take a light lunch—for example, a glass of milk and two crackers—at 10 in the forenoon and 3.30 in the afternoon. Eat no raw fruits or vegetables for six months (must be cooked).

You will note that the diet calls for eight prunes, five figs, one whole grapefruit, etc. The fact that the quantity of laxative foods is specifically designated makes the list more valuable. In order to cause a rapid gain in weight in undernourished individuals, a mixture of six ounces of milk (120 calories), one ounce of cream (60 calories) and half ounce of Dextrimaltose (40 calories) are ordered six times a day, thus adding 1,320 additional calories to the day's rations. Patients frequently gain twenty or more pounds in six weeks under this dietetic regime.

The object of a tepid sponge or shower bath in the morning on arising is twofold: aside from the hygienic effect of the bath, equal benefit is derived from a series of light, muscular exercises required in a vigorous, Turkish towel rub. These include bending, stooping and rotating movements.

Failure to make satisfactory progress is frequently due to lack of systematic and properly graduated exercises. A single violation in the way of overindulgence may retard progress a week or more. Patients are always cautioned not to eat when tired. A rest of twenty minutes before eating in weak and nervous individuals does more to prevent digestive disturbances than any drug would do.

To cure spastic constipation, it is necessary to direct treatment primarily to the relief of the colonic spasm and the associated catarrhal colitis. Various measures are employed for this purpose. Among these may be mentioned the relief through psychotherapy of anxieties, worries and apprehensions for the sake of improving the general nervous system; the application of hot, moist compresses to the abdomen; a suitable non-irritating, laxative diet; the avoidance of enemas and strong purgatives; the use of mineral oil, agar, psylla seed or a combination of them as a substitute for the more drastic purgatives, and antispasmodics such as tincture of belladonna, either plain or in combination with sodium bromide as a sedative, and spirits of chloroform as an antifermentative. These measures were all indicated in this particular case as the stasis and dilatation of the colon were the result of colonic spasm.

In cases of spastic constipation occurring in thin enteroptotic individuals, following the rest and fattening cure, a suitable support should be worn to relieve the mechanical defect resulting from gastroenteroptosis which interferes with proper functioning of these organs. However, a support should not be applied in the case of a female with coexistent uterine retroversion or prolapse, or if the abdominal viscera are held down by adhesions, a matter which can be easily determined during a fluoroscopic examination by examination by exerting pressure with the palm of the hand over the suprapubic area and noting the degree of elevation produced by this pressure.

Frequently the nervous and mental symptoms dominate the clinical picture in the advanced form of the disease. These often are in the nature of maladjustment, introspection, depression, phobias, obsessions, etc. For purposes of reëducation and readjustment, books along the line recommended in the list of instructions often prove most helpful, especially when resorted to in connection with other psychotherapeutic measures. In these nervous individuals one of the commonest causes of constipation is spasm of the anal sphincter with rectal dilatation and impaction (dyschesia). Mechanical dilatation of the sphincter in addition to the general routine treatment is necessary to cure this form of constipation.

The injurious effect of the indiscriminate use of cathartics or purgative drugs which act by irritating the intestinal mucous membrane has already been emphasized. Preparations which have a soothing effect and act by mechanically stimulating peristalsis, e. g., mineral oil, agar, psylla seed, should be employed instead of those which act as chemical irritants.

Unfortunately pharmaceutical chemists have foisted upon the public as well as the profession many preparations combining both classes of drugs. In this venture phenolphthalein, the ingredient which is a constituent of many of these compounds, has proved to be generally toxic and locally irritating. Such combinations are not only pharmacologically unsound but physiologically incompatible and therapeutically harmful, since any irritating drug, and especially phenolphthalein, will not only prevent the possibility of curing spastic constipation but will actually aggravate the associated colitis, and thus increase instead of decrease the tendency to spasm and constipation.

Colonic irrigation, like many other therapeutic fads, has come down to us from the early Egyptians, who practiced it quite extensively. Since then it has been exploited periodically as a sovereign remedy for many ills. However, it never withstood the supreme test of time. At present we are just about emerging from one of these cyclic periods. Based on personal experience, my opinion is that enemas or high colonic irrigations should be employed only as temporary measures and never as a routine procedure.

Obviously only the more advanced and complicated cases require treatment as elaborate as the cases herewith presented, but unfortunately due to neglect, either on part of the patient or the physician, too many finally reach this advanced stage. Earlier in the course of the disease, before stasis and dilatation of the large bowel develop with concomitant toxic neurosis ("enterics"), simpler measures suffice. They may not require institutional management and care. However, they do require modified rest combined with appropriate diet, suitable hygiene and proper medication

somewhat on the order of those prescribed for patients who are about to be placed on their own responsibility after institutional care.

The directions as stated should preferably be typewritten and specific in every detail. Education plays a role quite as important in effecting a cure of this condition as it does in tuberculosis and diabetes. Preventive measures based on education and early training in regard to the formation of correct habits, a knowledge of the science of nutrition, the dangers of dietetic fads and self-medication, especially the misuse and abuse of enemas and purgative drugs, would be of inestimable value in reducing the incidence of chronic spastic constipation with all of its attending evils. The statement has been made that if all the drugs used as purgatives were taken off the market constipation would soon be reduced 50 per cent.

Since it is along the line of preventive medicine that the best results can be obtained, attention to the subject must begin with the habit-forming age of infancy and early childhood and continue throughout the school period. By this method of approach it is possible to prevent much suffering and disability in later years, in addition to the economic loss sustained through the disability and the effort to regain normal health.

After a careful clinical analysis of the subject, one is impressed with the fact that constipation is not a simple minor ailment as ordinarily regarded by both the public and the profession. On the contrary, it constitutes one of the major medical problems and deserves much more serious consideration and more skillful and scientific management than has been accorded it heretofore. The public needs to be awakened to a fuller realization of these facts and the medical profession would find in this field an excellent opportunity to do some effective, constructive educational work in the interets of preventive medicine and public health.

THE TREATMENT OF PERNICIOUS ANEMIA*

By

S. M. GOLDHAMER, M.D.
and
F. H. BETHELL, M.D.
ANN ARBOR, MICHIGAN

THE treatment of pernicious anemia is dependent upon the stage of the disease at which the patient is first observed and the degree of involvement of the different organs. At present it has not been demonstrated that there is any correlation between the anemia and the neurological manifestations. The therapy of these two aspects of the disease, while applied simultaneously, is to a certain extent independent. There appear to be five factors which may produce the blood picture of pernicious anemia. It is generally accepted that the substance necessary for the maturation of the red blood cells is formed from the interaction of (1) an extrinsic factor (food) and (2) an intrinsic factor present in the stomach. The resulting product (3) is absorbed from the intestine, (4) stored in the liver, and (5) released to the body tissues for utilization when needed. Any disturbance of this mechanism at the point indicated by the numbers will produce a macrocytic anemia. The type of anti-anemia treatment, therefore, depends upon which factor or factors are contributing to the cause in each given instance. In the Addisonian type of pernicious anemia, Castle has demonstrated that the essential lesion is a lack of the intrinsic factor in the gastric secretions.

TREATMENT OF THE ANEMIA

For the average patient in relapse, without complications, one-half pound of beef, calf's or other *liver* should be administered daily. The liver may be taken raw and finely ground, or it may be cooked in any way which makes it palatable. Since the active principle is soluble in water, any liquid used in preparing the meat should be added to the liver when it is eaten. When *liver extract* is prescribed, the amount derived from 600 gms. of liver may be dissolved in water or a suitable liquid, and taken daily. There are many satisfactory preparations of liver extract available commercially. Before prescribing any particular type, however, the physician should satisfy himself that the preparation is of known potency as determined by clinical tests. These liver extract preparations physically may be dispensed in capsules, liquid form or powder extracts, which may have been treated with stomach enzymes or prepared from autolyzed liver. Regardless of the type of extract, maximum doses should be given until the blood reaches a normal level. The maintenance dosage can be determined by frequent observations of the blood.

A preparation equally as effective as is liver is the oral preparation, *desiccated defatted hog stomach.* Usually 40 grams daily are administered during relapse. When the blood is within normal limits, a maintenance dose of 10 to 20 grams may be administered daily.

Recently, *parenteral liver therapy* has gained wide prominence because of its relatively increased effectiveness in small amounts and the decreased cost to the patients. Further, if the anemia is due to a failure of absorption or storage, oral administration may be useless, whereas parenteral therapy is most beneficial. The dosage of parenteral extract depends upon the initial amount of liver or liver extract used.

The intravenous extract (Parke Davis) prepared from 100 grams of fresh liver is administered in an aqueous solution of 20 c.c. at weekly intervals until the blood reaches a normal level. Maintenance treatments are then given at three to six-week intervals, depending upon the state of the blood. The same preparation may be given intramuscularly in smaller doses. The initial injection is 10 c.c., then semi-weekly treatments of 4 c.c. until a normal blood count is obtained. The maintenance dose is 4 to 6 c.c. weekly, or less depending upon the individual. Patients easily can be trained to administer the intramuscular treatment to themselves, thus further decreasing the cost to them. There is a number of other equally effective commercial liver extract preparations available for intramuscular use.

*From the Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan, Ann Arbor, Michigan.
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If the patient has a profound anemia or severe complications, multiple blood transfusions (600 c.c. per transfusion) are indicated in addition to the anti-anemia therapy. Some clinicians advise the use of such therapeutic adjucts as iron and vitamins, but it is questionable whether they have any specific effect on the blood in pernicious anemia.

The blood count usually reaches normal in from four to twelve weeks with adequate therapy, depending upon the severity of the anemia when the patient first is seen and other factors, such as presence of infection. When the red blood cell count is normal, the amount of medication may be reduced, and any further changes can be made with periodic blood examinations as guides. Clinically, relapses manifest themselves by a loss of appetite, sore tongue, an aversion for oral anti-anemic therapy and the signs and symptoms of anemia. *It is during this interval that parenteral treatment* becomes most valuable.

While the above mentioned types of therapy appear to be specific for the anemia of pernicious anemia, they have little or no effect on the majority of secondary anemias. For this reason a correct diagnosis is extremely important. A therapeutic test with liver or its derivatives, may cause loss of valuable time in anemias due to chronic hemorrhage, nephritis or cancer.

TREATMENT OF SPINAL CORD AND CEREBRAL MANIFESTATIONS

One of the most frequent complications is an infection of the genito-urinary tract, which is present in about 40 per cent of the cases. If the infection is mild, urinary antiseptics alone are given in addition to forcing fluids (5,000 c.c. daily). If a *"cord bladder"* is present (retention or incontinence), more drastic measures are indicated. The bladder may be manipulated by normal pressure at six-hour intervals, and if this is unsuccessful, "mecholin" may be given. It may be necessary to catheterize the patient daily or to insert an inlying catheter. For irrigation of the bladder, a 1:1000 solution of acetic acid has proven most effective. Return of normal function of the bladder is not hindered when the catheter is removed.

Careful attention must be given to prevent *decubitus ulcers*. These may form over any of the bony prominences (sacrum and hips), or from pressure against the bed. Ulcerations may appear in the intergluteal folds. Besides the systemic treatment, reddened skin areas may be painted daily with collodion solution or Balsam of Peru. Exposure to the light from a carbon filament *bulb* tends to hasten healing of the ulcers. If the ulcers are deep or gangrenous, surgical intervention is necessary. The infection may then be cleared up with boric or acriflavine dressings. An extensive ulceration should not necessarily cause discouragement, lesions having been found to heal even after sloughing of parts of the sacrum and surrounding tissues.

Disturbed locomotion. When the patient is unable to control his extremities, passive and active exercises are indicated. The muscles may be massaged, coincident with the application of dry heat. The patient should be encouraged to try to walk with aid. The floor may be laid out in squares and the patients taught to place their feet in the designated blocks. Occupational therapy is most beneficial in developing control of the fingers, as well as relieving the monotony of inactivity.

Cerebral involvement varying from a mild irritability to severe psychoses is common in pernicious anemia, as it occurs in over 50 per cent of the cases. The peculiar mental reactions of patients with pernicious anemia must be appreciated by those nursing them, so that there will be no opportunity for mishandling the patients. Usually mental symptoms will disappear with routine therapy.

TREATMENT OF THE GASTRO-INTESTINAL TRACT

Inasmuch as the cause for the *glossitis* is unknown, no specific therapy is known. Alkaline mouth washes are usually helpful. Dilute hydrochloric acid, 4.0 c.c., in a glass of water with meals is beneficial for the relief of epigastric distress and distension in some patients, but its routine use is unnecessary. The distension may also be aided by pituitrin (1.0 c.c. obstetrical) and exhibition of a rectal tube.

One of the most troublesome features is *constipation*. A routine therapy which has proven satisfactory in our service is liquid petrolatum, 30 c.c. b.i.d., cascara sagrada, 0.65 gram, before retiring, and the establishment of normal habit of defecation. Obstipation may be relieved by glycerine or soap suds enemas.

GENERAL MEASURES

The *diet* should be liberal and well-balanced and should include meat, eggs, greens, vegetables and fresh fruits. Concentrated vitamins can be added for their questionable influence on the spinal cord disease. Ordinarily, when a therapeutic remission is induced the patient's appetite increases greatly and, as a result, the caloric intake, consisting of a wide variety of foods, is so increased that special dietary measures are unnecessary. It has been found that it is not necessary to limit the amount of fats or carbohydrates unless they cause indigestion.

The details of ordinary *hygiene* should be carefully followed. Focal infections should be eliminated whenever possible. However, the teeth should not be removed indiscriminately unless one is fairly certain that those remaining are adequate for the proper chewing of food or that a suitable set of artificial teeth can be provided.

As a final word, and it cannot be emphasized too much, it is necessary *to establish the proper diagnosis*, to use a known, potent anti-anemia preparation, and to impress the patients with the necessity for continuous therapy throughout life in order that relapses may be prevented, and to warn them of the grave dangers of complications.

SECTION VI—*Abdominal Surgery*

THE UNCOMMON TUMORS OF THE LARGE INTESTINE

By

J. ARNOLD BARGEN, M.D.*

and

CLAUDE F. DIXON, M.D.*

ROCHESTER, MINNESOTA

CARCINOMA is the commonest malignant tumor of the large intestine. Sarcoma occurs considerably less frequently. These two types of malignant growth represent by far the large majority of new growths which come under the observation of the diagnostician and the surgeon. Adenomatous polyps of the colon and rectum are, themselves, of sufficiently frequent occurrence to warrant description and discussion by themselves. Various aspects of these lesions have been reported previously. As diagnostic methods improve and routine examination of the colon and rectum are undertaken in all cases in which there is any form of intestinal dysfunction, other less common tumors are encountered, many of which are benign.

At first thought it might seem that these less common tumors are so rare, and, since they are usually benign, so innocuous as hardly to deserve mention, but when it is recalled that occasionally benign tumors assume immense proportions, cause obstructive phenomena, may be associated with anemia and bodily depletion and a patient may be denied adequate treatment occasionally because such tumors were thought to be malignant and inoperable, a careful study of a group of such tumors seems timely.

Some of these rare tumors may be malignant. In such instances the malignant process usually progresses slowly and causes injury by extension into adjacent tissues. The rare benign tumors of the large intestine may remain symptomless until they assume proportions sufficient to interfere with normal mechanical function of the bowel. Occasionally they produce such complications as intussusception and consequent obstruction. Therefore, it is conceivable that patients have harbored such growths during their entire lives, have never had symptoms from them and have died of other causes with these growths undiscovered. Other such growths, however, have been brought to our attention very forcefully, and occasionally, because of their size and the other features mentioned, have been thought to be incurable.

Unusual pathologic types observed include: fibroma, fibromyoma, fibromyxoma, fibromyxomyoma, adenofibromyoma, fibroleiomyoma, myoma, adenomyoma, angioma, lipoma, cholesteatoma, paraffinoma, papilloma or villous tumor, teratoma, glioma, chordoblastoma, endothelioma, dermoids and cysts of the cecum. Each type of tumor originates from the part of the intestinal wall which corresponds to the histologic structure of that tumor: for example, adenomas from the mucosa, fibromas from the submucosa and serosa, lipomas from the fat cells of the external coat and from the appendices epiplöicae, angiomas from the blood vessels of the intestinal wall, and myomas, according to most investigators, from the muscularis or the muscularis mucosa. Of the benign tumors reported in the literature, adenomas are the most frequent, angiomas the most infrequent and myomas comparatively infrequent.

SYMPTOMS

The group of tumors being discussed has no characteristically distinguishing symptoms. Their presence is usually unsuspected until there occurs mechanical occlusion of the intestinal lumen, until intussusception of the tumor into that part of the bowel which is distal to it takes place, or until volvulus of the involved segment occurs. All of the varieties occasionally produce intestinal obstruction; this is more commonly met in its partial or intermittent form. The partial type of obstruction may merge into an acute complete variety, or may be ushered in by an acute attack which subsides, only to recur at varying periods and then evidenced by paroxysmal cramps, abdominal distention or tenesmus. The attacks of obstruction vary in no way from the attacks of intestinal obstruction resulting from any mechanical cause, and usually characteristic, cramp-like attacks of colic occur, resulting from direct occlusion of the intestinal lumen by the tumor itself, from intussusception caused by the effort of the bowel to rid itself of the tumor, or from torsion and volvulus. The number of tumors varies from a single growth to involvement of all the colon, as it is involved in adenomatous polyposis. The tumors also vary in size from small, sessile elevations to huge pedunculated, solitary tumors which encroach on the intestinal lumen. When the growths are in the ascending or the transverse colon, often the first symptoms are those of obstruction; when they are in the sigmoid or upper part of the rectum, such growths are always more productive of discomfort and of derangement of function. Frequently they cause a sensation of fullness and produce dull pain or soreness in the left part of the abdomen. With growths in the lower part of the colon, and particularly in the rectum, urgency and frequency of desire to defecate, with unsatisfactory and incomplete evacuation, occur. Pedunculated rectal growths are likely to be extruded through the anus and, with extrusion, may be associated partial or complete prolapse of the rectum.

Diarrhea, in one form or another, usually is present at some time during the growth of a benign tumor; it

*Respectively of the Division of Medicine and of Surgery, the Mayo Clinic.
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varies in severity from intestinal irritation, with several stools per day, to a violent attack with ten or twelve evacuations daily. Usually blood is not present in the stools, although in a case of lipoma it is noted oftener than with other varieties of benign tumor. This is caused by ulceration of the mucous membrane overlying the growth and often results in profound anemia. A number of cases has been reported in which the clinical picture of malignancy has been mimicked by a benign tumor, usually of the lipomatous or angiomatous variety. Here, the secondary anemia, loss of weight and cachexia, which are incidental to disturbances of gastro-intestinal function, probably are largely responsible for the clinical picture.

TYPES OF TUMOR

Fibroma. Fibromas of the large intestine are extremely rare. They arise from the fibrous tissue found in the submucous coats of the bowel; types such as fibromyoma, fibroleiomyoma, adenofibromyoma, fibromyxoma and fibromyxomyoma have been described. Jansen, in 1886, probably reported the first true fibroma, a hard, mobile tumor, 8 cm. in diameter, in the descending colon of a woman aged thirty-five years. It was successfully resected. To the seven cases of fibroma previously reported from the Mayo Clinic, we should like to add one more striking case.



Fig. 1. Gross appearance of fibroma of cecum.

Case 1. A married woman, aged forty-six years, came to this Clinic November 13, 1931, because of a tumor in the right, lower quadrant of the abdomen, and occasional attacks of pain in this region. The pain had been present for about three years, never severe, occurring on quick motion or when turning in bed. In August, 1929, abdominal exploration was carried out elsewhere, with partial oöphorectomy. The woman seemed somewhat better after the operation, but the infrequent pains in the right lower quadrant continued. She felt positive about the presence of a tumor a year before her admission and felt that it had grown somewhat during that time. There were no associated digestive symptoms and the woman made no other complaints.

At the time of her admission, blood pressure was 120 mm. of mercury systolic and 80 diastolic; temperature 98.2 degrees F., weight 166 pounds (75.3 kg.), which was her usual normal. There was a firm, smooth, movable tumor in the right lower quadrant, about 12 cm. in diameter. We were struck with its unusual mobility. We were able to slide the tumor along in the left loin below the kidney; the latter could be felt separately. *Roentgenologic* examination disclosed a hyperplastic lesion involving the cecum.

November 21, 1931, ileocolostomy was performed. January 23, 1932, right hemicolectomy was performed for a fibroma of the wall of the cecum, not involving the mucosa; the tumor was 6 cm. in diameter (Fig. 1). Recovery was uneventful and the patient has remained well.

Myoma. Pure muscle tumors are exceedingly rare; most tumors designated as such contain varying amounts of muscle and fibrous tissue. The first true myoma of the rectum was reported by Vander Espt in 1881. Hunt, reviewing the literature back to 1872, classified twenty cases as examples of myoma or myofibroma of the rectum. He added reports of four cases encountered at the Mayo Clinic. Of this total of twenty-four patients, eleven were males and thirteen females; the youngest patient was aged twenty-one years; the oldest, eighty-five years. These tumors may assume great proportions; the largest we found was 15 cm. in diameter. Marked constipation, hemorrhage, and rectal pain were the predominating symptoms. Complete obstruction occurred in three instances. Malignant change has been known to develop in these tumors. The tumors are cellular and tend to recur after enucleation. Furthermore, after repeated removal, it has been noted that successive examination of the specimen discloses increasingly greater cellular infiltration and malignant change. Such a case was reported in 1932[17] and another follows:

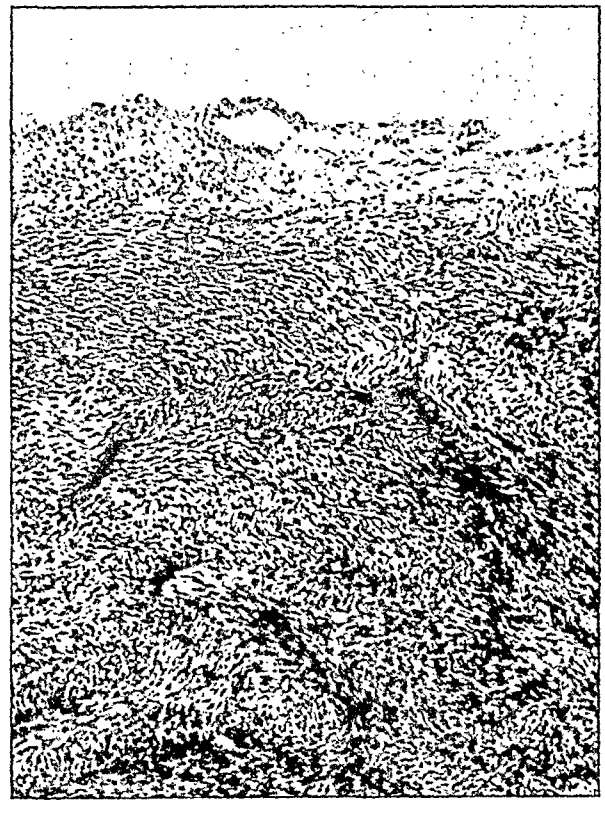


Fig. 2. Microscopic section of myosarcoma (x 75).

Case 2. A man, aged fifty-one years, a confectioner, came to this Clinic, April 10, 1931, because of a small lump behind the anus. He had first noticed the lump about 1922, and it had slowly, gradually, enlarged to a diameter of about 7 cm. by August, 1929. The tumor did not cause pain. At that time it was removed elsewhere and was designated as a "shell tumor, suggestive of cancer". The wound healed properly; there was no drainage and no recurrence of the tumor for eighteen months. About that time, the man noticed a painless lump the size of a walnut in the same region as the first tumor. When the patient was examined at this Clinic several months later, the same rounded tumor was found at the posterior wall of the anus, and measured about 3 by 3 cm. The lesion appeared to be beneath the submucosa; there were no ulcers and no bleeding. Over it was the scar of the former operation.

April 14, 1931, under sacral anesthesia, the tumor was removed by resecting the left half of the anus. Pathologically, the lesion was a myosarcoma, graded 2.

The man returned in February, 1932, at which time the re-

current lesion was about as large as it had been in April, 1931. Single-barrelled colostomy was performed, and the entire rectum and its perirectal structures were removed by combined abdominoperineal resection. Pathologically, the lesion was 3 cm. in diameter and again was a myosarcoma graded 2 (Fig. 2). There was no involvement of lymph nodes. The patient made an uneventful recovery.

Adenomyoma. Spencer, in discussing a paper by Lockyer, in 1913, probably was the first to refer to a case of adenomyoma of the sigmoid. In 1920, Cullen reported four cases of adenomyoma of the sigmoid, two from own experience and two from the literature. Ten cases were reported from this Clinic in 1932.[17] Nine of the adenomyomas occurred among women between the ages of twenty-seven and forty-eight years; the tenth one occurred in a man aged eighty years. The tumors of the women were at the sigmoid, and might have been implants or extensions from former pelvic lesions. All were found in relation to pelvic disease, and in several cases, by their annular nature, produced obstruction of the sigmoid. Several of the tumors were possibly of ovarian origin. Enucleation was possible in some cases, but resection of the sigmoid was necessary in others. Adenomyoma of the recto-vaginal septum occurred fairly frequently, but consideration of them has been omitted here. The adenomyoma of the man aged eighty, occurred as a hard, postanal tumor that was diagnosed preoperatively as carcinoma.

Angioma. This is perhaps the rarest type of tumor found in the large bowel, and varies in size from a small nevus to a pedunculated type which grossly may attain considerable size. Apparently the tumors are of congenital origin. Involvement of the whole colon in an angiomatous process has been noted, but it is extremely unusual to find this type of growth in the colon except in its lower segments. The tumors usually arise in the submucosa, but Buie and Swan found the origin of the tumor in the serosa in one of their cases. Ulceration occasionally takes place with resultant hemorrhage, but there is otherwise little about these lesions to suggest their pathologic nature. The angiomas described have been hemangiomas. Of those cases of angioma for which operation was performed at this Clinic, one of the tumors was in the wall of the cecum; it was accidentally discovered in the course of an operation for gallstones. One occurred in the splenic flexure, one in the sigmoid, one at the recto-sigmoid and one in the rectum. The latter three were diagnosed as polyps preoperatively, and the one at the splenic flexure as carcinoma because of the type of roentgenographic filling defect.

Lipoma. Lipomas of the large intestine should be considered to be only relatively rare, for after adenoma (not considered in this paper) lipoma is the most frequently encountered benign tumor of the gastrointestinal tract. However, as Comfort pointed out in 1931, only seventy-four symptom-producing lipomas of the large intestine had been reported in all medical literature available to him. The diagnosis has been made before operation only in exceptional cases. It is rare that the diagnosis can be more accurate than that of a benign tumor, although in some instances, in which the tumor is visualized through the proctoscope, or in which it has prolapsed to the outside, its character is apparent.

The age of patients with lipomas, the frequent appearance of blood in the stools, and the loss of weight, together with the attacks of obstruction, make difficult the differential diagnosis between lipoma and carcinoma.

Cholesteatoma. One variety of tumor, apparently never before reported as having been found in the large bowel, namely, cholesteatoma, was first recorded by Humiston and Piette, in 1925. In their case, the tumor was situated in the cecum; in a review of the literature they failed to find a report of any other tumor of this epidermoid variety in this situation. A cholesteatoma is described as a "cystic tumor with thin epithelial lining, and a content which is formed of epithelial cells and cholesterol". Tumors of this variety presumably originate from misplaced, embryonic, epidermoid germ cells. Similar changes occasionally are produced by chronic inflammation.

The cecal cholesteatoma, described by Humiston and Piette, was found in a young man who presented typical symptoms of subacute appendicitis; at exploration there was found an inflamed appendix with an encysted tumor in the outer wall of the cecum, which tumor did not connect with the lumen of the bowel and was easily enucleated. Gross and microscopic examinations confirmed the diagnosis of true cholesteatoma of the cecum.

Dermoids. True dermoids of the rectum occur very rarely, although dermoid cysts and tumors in the perirectal spaces are not uncommon. Our contribution is not concerned with the postrectal dermoids, those of the rectovaginal septum, nor those invading the rectum from nearby structures, as for example, from the ovary. True dermoids may arise in the rectal wall; for this reason they produce symptoms relatively early. They may be pedunculated and so protrude from the anus, or produce obstruction by invagination of the wall of the bowel. The first sign may be protrusion of hair from the anus. The patients may suffer from constipation of obstructive type, marked tenesmus, and, at the time of defecation, the tumor may present at the anus. The tumor may consist of skin covered with hair and sebaceous follicles, enclosing fat and fibrous tissue. Dermoid cysts have been adequately described by Bensuade and Rachet, Port, Saphir, Maingot, and Danzel.

Teratoma. Although there is no sharp line of demarcation between dermoids and teratomas, in the strictest sense, a teratoma is a tumor containing tissue and fragments of viscera and without the cystic fluids of dermoids. In Fried and Stone's case, the lesion was a teratoid mass of mixed tissue, and instead of being a cavity lined with skin, it was a solid mass covered by skin. The tumor swung freely in the lumen of the bowel, attached by its pedicle to the posterior rectal wall. It was comma-shaped, with a smooth surface, and covered with small patches of brown hair. At one point, a hard, pearly-white object projected; it resembled a tooth. Microscopically, it was surrounded by cornified squamous epithelium, and it contained smooth muscle, connective tissue, fat, sweat glands, bone and hair follicles.

Cysts of the cecum. Few instances of this condition have been reported. McAuley reviewed the literature up to 1923, and found reports of eleven cases; he reported another case. Bazin, in 1925, added still another. McAuley argued that the condition should be considered as a definite entity. In the literature there is a fair number of references to enteric cysts and other cysts of the intestine. Such cysts produce symptoms of obstruction, or are discovered at necropsy or operation. The condition they cause usually is diagnosed as irreducible intussusception; the diagnosis is not established until the resected specimen is examined.

Rath reported the case of a woman, aged forty years, in which the diagnosis was hydrops of the appendix,

but on exploration the mass was found to be a cyst of the cecum with its base 3 cm. distant from a normal appendix. Flick reported a case in which a large cyst had twisted itself on a pedicle 1.5 cm. long; the cyst contained bloody fluid. This had brought on the clinical picture of acute disease within the abdomen.

In the years for which the records of this Clinic were reviewed, two cysts of the cecum were found.

Papillomas or villous tumors. These tumors have been variously designated as papillary tumors, villous carcinomas, villous polyps, papillary polyps and papillary adenomas. Whether they should be included here is doubtful. We mention them only for the sake of completeness.

Paraffinoma. This tumor results from injection of paraffin. When the tumor is in the lower part of the rectum, the injection has been made for hemorrhoids.

Chordoblastoma and glioma. Although these are not primarily rectal tumors, occasionally the symptoms they cause are referable to the rectum; hence, they should be mentioned in any discussion of unusual rectal new growths.[21]

Endothelioma. Endotheliomas are similar to gliomas in origin and clinical characteristics. They have been found to remain quiescent for many years and then, suddenly, for inexplicable reasons, to grow with great rapidity. The symptoms depend primarily on the size, situation and direction of extenison of the tumor. Usually they are superficial. When they arise in the rectum proper, their symptoms are those of obstruction; their diagnosis usually is suggested by digital and proctoscopic examination. Because of the relatively early invasion of the spinal cord by all tumors which arise from neural structures, pain in the region of the sacrum and coccyx is common, and by impingement on the sacral and lumbar plexuses, the tumors may give rise to sphincteric disturbances and to paresthesia in the perianal region and in the region about the urethra. Sensation of incomplete evacuation, dragging and heaviness in the pelvis and painful defecation also may be observed.

Roentgenograms are of value in revealing spina bifida or other bony defects in these regions or they may reveal bony structures and teeth. At times, these neural tumors result in the erroneous diagnosis of sciatica, coccygodynia, arthritis and rectalgia of other types.

TREATMENT

Treatment of all of these lesions is surgical. In some patients, local excision is all that is required. This is particularly true of those benign tumors which can be seen by the sigmoidoscope. Sometimes lipomas, fibromas and other tumors are on a pedicle; then fulguration with the electric cautery is the treatment of choice. Many times, however, when lesions are above the rectosigmoid, radical resection is the appropriate treatment because the important question of the malignant nature of the tumors cannot be settled before they are removed.

Thus, the rectal fibromas were excised locally, but for the cecal fibromas ileocolostomy and subsequent right hemicolectomy were performed.

In reviewing the records of the cases of myoma, local recurrence with repeated excision was common. Specimens removed on successive examinations were recorded by the pathologists as being examples of myoma, cellular myoma, and malignant myoma. Hence, it seemed wise, in the case of the recurrent myosarcomas, to perform radical resection as described in Case 2.

Angioma, because of the size it may attain and its clinical similarity to carcinoma, usually requires radical excision. Cholesteatoma may be enucleated from the colonic wall without radical resection of the intestine. Because of their tendency to recur, villous tumors are best treated by radical extirpation. The paraffinomas reported in the literature were both resected; the lower end of the anal canal with sphincters was preserved and results were completely satisfactory. For the neurogenic lesions, excision is the usual treatment. In the case of chordoblastoma, excision of the lesion and insertion of radium have given satisfactory results.

When feasible, the treatment of choice of endotheliomas is complete surgical extirpation. The posterior approach, with at times removal of the coccyx and lower sacral vertebrae, may be necessary. Radium and roentgen rays have supplemented surgery with indefinite results. Prognosis in cases of the malignant types of tumors is unfavorable, generally, and is patricularly bad when associated with meningocele.

The treatment of dermoids consists of complete removal and dissection, with the tumor intact. However, removal of the sac of a large dermoid may be facilitated by first evacuating the content. Exposure of the tissues to the content of the dermoid usually will set up a violent inflammatory condition. Every portion of the wall of the cyst must be removed; otherwise the wall will not close and the cyst will re-form. Complete removal and not drainage is essential for permanent cure. Cysts of the cecum, because of the mechanical difficulties which they produce, should be removed surgically.

This brief review of uncommon tumors of the large bowel, if for no other reason, seems justifiable because such tumors occur just often enough to warrant their possible presence being kept in mind when dealing with tumors generally.

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SOME PRINCIPLES IN THE TREATMENT OF SEPTIC CONDITIONS FOLLOWING ABDOMINAL DISEASES*

By

JAMES NORMAN COOMBS, M.D., F.A.C.S.
PHILADELPHIA, PENNSYLVANIA

THE septic complications of abdominal diseases are often the most difficult the surgeon is called upon to treat. The early local manifestations of infections within the abdomen, such as the inflamed appendix and gall bladder, give more or less well defined symptoms and signs that indicate the usual surgical procedure. However, after delay in diagnosis and treatment when such an infection extends beyond its local confines by perforation or invasion of the blood stream, increasing difficulty arises as to the type of surgical treatment to be instituted. Often, instead of the treatment of a local disease, one is at once confronted with a septicemia, a general peritonitis or both. The treatment of this

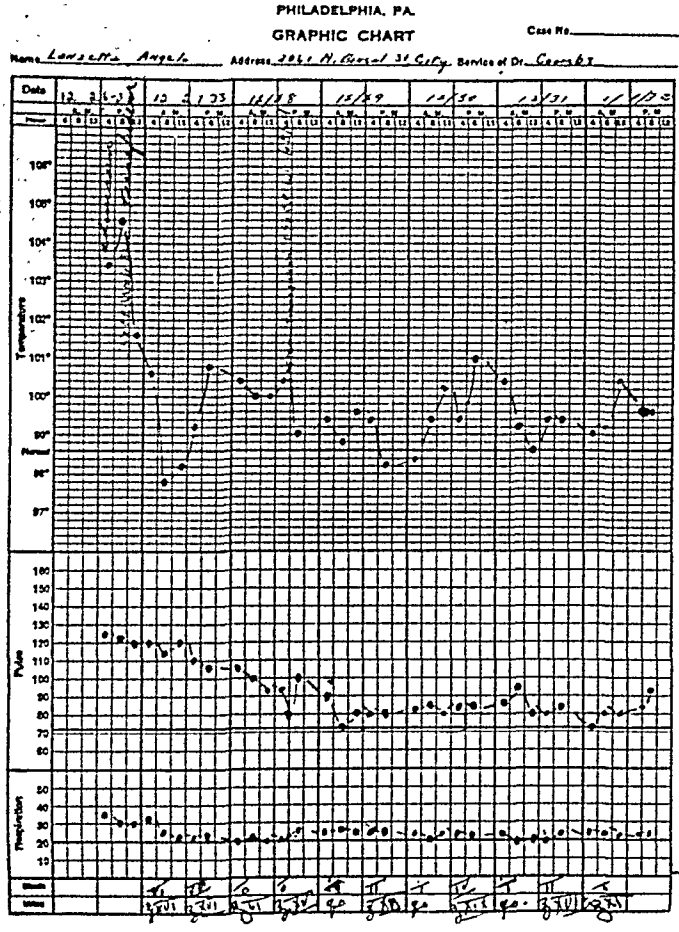


Chart I, Case 1. Chart showing time of the blood transfusions and result.

patient then naturally is supportive, rather than curative.

On the surgical service at Temple University Hospital, such patient routinely is given continuous hypodermoclysis (2½ per cent glucose in normal saline solution) with the purpose of administering 3,000 c.c. per twenty-four hours. Hypodermoclysis may be continued for days. To maintain the intake of fluid, the needles must be changed to a new position every twenty-four to thirty-six hours, using both pectoral regions or the subcutaneous tissue of the thigh. The rate of flow should be regulated by raising or lowering the receptacle containing the glucose and saline solution, so that the tissues do not become engorged and thus produce discomfort to the patient.

In blood stream infection, we have found that repeated blood transfusions are of distinct value; the patient receives 250 to 300 c.c. of whole blood by direct transfusion every third day until the temperature recedes or upon general systemic improvement. It has been noted that following a transfusion the patient may experience almost immediate relief, with gain in strength and drop in temperature. This is illustrated in the following case:

Case 1. A boy age 14, was admitted to the surgical service extremely ill with general abdominal pain, nausea, vomiting, diarrhea, temperature 104.3 F. and pulse 130. There had been a chill a few hours before admission; he had been sick for four days. The face presented a dusky hue, the eyes were sunken, and the lips parched. The abdomen was rigid throughout with beginning distention, the maximum tenderness being in the lower abdomen. Realizing that we were dealing with an advanced peritonitis due to a virulent infection and that operation for drainage would be hazardous, "Ochsner Treatment" and blood transfusion were ordered. The patient received 190 c.c. of whole blood within a few hours after admission. The following morning there was marked improvement in the well-being of the patient. The temperature was 97.4 F., the pulse 110 and respiration 25. At the end of thirty-six hours, the diarrhea had ceased, the distention and rigidity were less. On the third day after admission, he was given a non-specific immuno-transfusion of one hundred and fifty cubic centimeters of whole blood taken from a suitable donor who had been given intravenously a vaccine containing twenty-five million para-typhoid bacilli A and B, and fifty million typhoid bacilli. Carefully checked blood counts were taken on the donor following reaction to obtain blood at the time when leucocytosis was greatest. This patient showed continued improvement, with cessation of abdominal symptoms. He was discharged from the hospital on the twenty-first day after admission and has remained perfectly well.

Blood transfusions in septic cases may be continued indefinitely until improvement. In order to avoid untimely reactions, it is our practice, regardless of the time element and type of donor, to cross-agglutinate blood specimens of the recipient and the donor before each transfusion.

For the relief of vomiting, upper abdominal distention and to combat ileus, the application of suction syphonage by way of an in-dwelling nasal catheter attached to a Jutte or Levine duodenal tube, has been of distinct advantage. Dr. Gerald H. Pratt[1] of this Clinic has devised an ingenious evacuator using the principle of hydraulic suction; this apparatus is both simple and efficient (Figure 1).

Stomach and upper intestinal contents, including gases, may be aspirated with ease, rendering the patient comfortable by reducing intra-abdominal tension and thus aiding respiration. Vomiting ceases with the continuous aspiration. To relieve thirst and the constant desire for drink so common in peritonitis, clear fluids may be given by mouth, knowing, of course, that they will be immediately syphoned off. In paralytic ileus associated with peritonitis or local intra-abdominal suppurative processes, suction syphonage will drain

*From the Department of Surgery, Temple University School of Medicine, Philadelphia.
Submitted July 23, 1934.

the upper intestine of its toxic products and gases and in the great majority of instances will obviate the question of enterostomy.

With the advent of localization or attempt at localization of the infection on the part of the patient, caution must be exercised as to when, and when not, to operate. It must be borne in mind that operation, in the very ill patient before complete localization of inflammation has occurred, may break down recent barriers and open new avenues of infection. If drainage is desired, the most dependent positions are to be considered with the smallest incision and the least manipulation.

should be considered on account of their simplicity and dependent position.

Pylephlebitis or *portal thrombophlebitis*, a most dreaded complication, follows infection in areas drained by the portal system, most commonly the appendix, the onset being marked by severe chill, sweat, and temperature 104 to 105°, followed by recurrent chills with sweat and high fever. The liver becomes enlarged and tender. There is increased blood bilirubin and at times jaundice. According to Babcock[4] pylephlebitis causes 5 per cent of all deaths following acute appendicitis. The mortality from the condition itself is over 90 per cent.

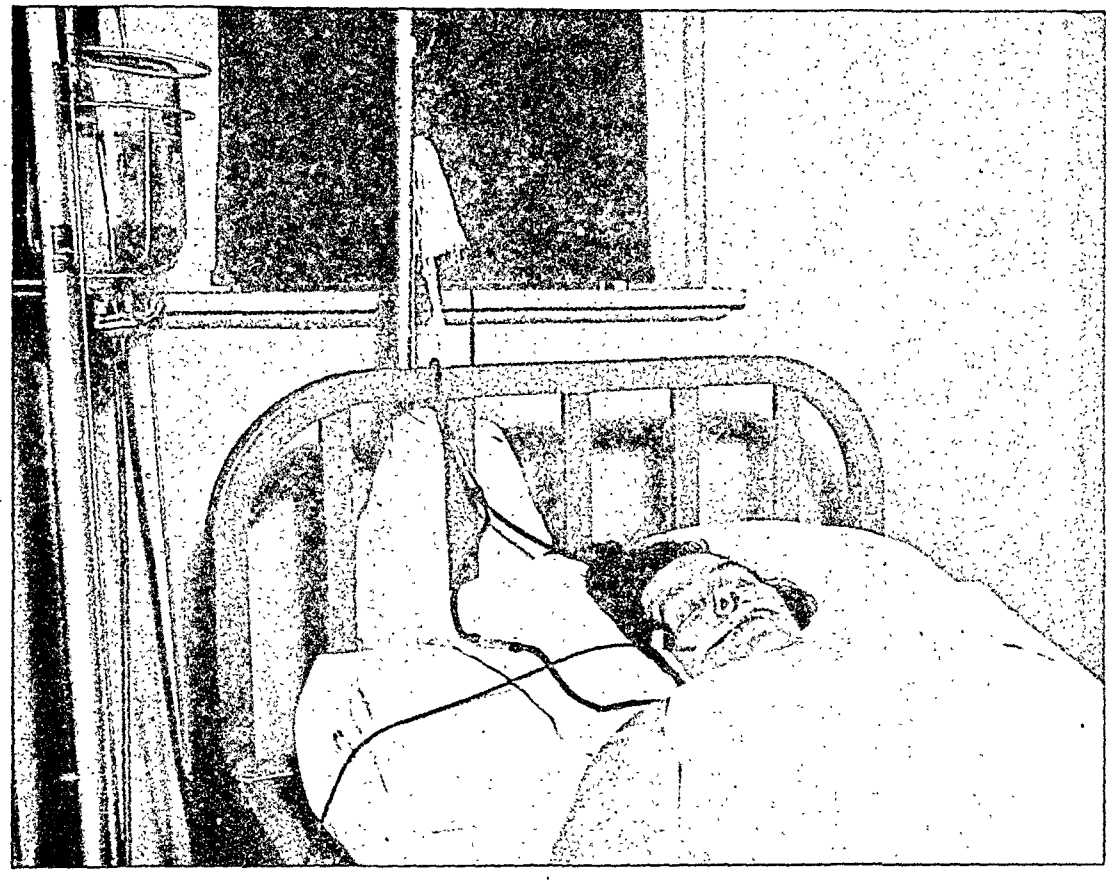


Fig. I. (a) Continuous hypodermoclysis, with "Y" connection allowing flow to needles introduced in both pectoral regions.
(b) Jutte tube introduced through the nose attached to evacuator at the bedside to syphon stomach and upper intestinal contents.

With a fully-formed abdominal abscess, extreme care must be employed at operation to avoid contamination of the peritoneum. Extra peritoneal drainage should be practiced. This can usually be established by opening abscesses within their attachment to the parietal peritoneum. (Figure 2.) The plan[2] is to make an incision over the mass in line of their fibers, exposing the parietal peritoneum. Finger exploration will guide one to the point of maximum fixation of parietal peritoneum to the mass or to a point of softening. Here the finger may be introduced into the abscess cavity and adequate drainage instituted.

For the pelvic abscess in women, posterior vaginal section should be done for drainage. Pelvic abscess in the male may be reached by way of the rectum. As outlined by Burnett,[3] the most important steps are accurate diagnosis and adequate drainage under vision to prevent peritoneal contamination.

In patients gravely ill from peritonitis secondary to perforative appendicitis, operations for vaginal drainage in the female and rectal drainage in the male

The treatment consists in giving large quantities of glucose to combat hepatic failure, and repeated blood transfusions to support the patient. Glucose may be given by continuous hypodermoclysis or intravenously, using a more concentrated solution at intervals, or a less concentrated solution by continuous drip through the tied-in vein cannula. With the cannula in place, blood transfusion may be given without otherwise disturbing the patient.

The operative treatment may be of little avail, although exploration seems indicated in certain prolonged cases in an attempt to evacuate localized liver abscesses that are accessible, or the opening and drainage of thrombosed veins leading from the focus of infection.

Subphrenic abscess is one of the late complications of intra-abdominal suppurative processes. Subphrenic infections, however, may occur early as a part of a general peritonitis, as is so often seen at the post-mortem table in the early, fatal cases of peritonitis. Ochsner[5] points out that infections of the subphrenic

space occur much more frequently than is commonly supposed. Fortunately, the majority of such infections subside spontaneously and may never be diagnosed, unless due to the continuation of the septic manifestations, the possibility of the existence of the subphrenic lesion is considered. In Ochsner's experience, only 30 per cent of the subphrenic infections actually proceed to suppuration. The remaining 70 per cent subside spontaneously.

X-ray examination with the patient in the erect position and also lying on the well side. One gets an almost certain diagnosis, not only of the abscess but of adhesions of the liver to the diaphragm, indicating the position of the abscess.

The extension of subphrenic abscess either by contiguity and continuity of tissue or by perforation may occur in late cases and in cases improperly drained. A patient recently on our service, debilitated from per-

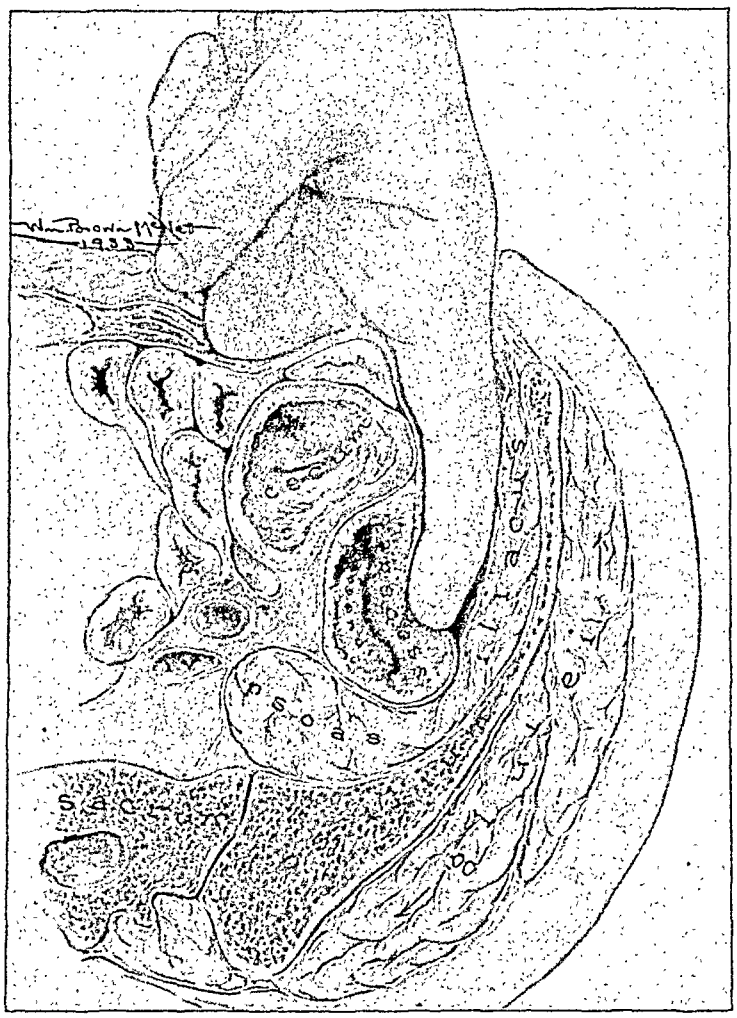


Fig. 2. The rectro-peritoneal evacuation of an appendiceal abscess.

The following case illustrates this fact: A female, age 40, who had a previous pelvic operation, was admitted to Temple University Hospital, March 14, 1934, *with diagnosis of uterine* fibroids. An abdominal hysterectomy was performed with difficulty on account of massive adhesions. Following operation, the patient ran a septic temperature for six weeks. Wound infection occurred early and was drained. Due to the persistence of the fever and debility of the patient, an X-ray examination of the abdomen was ordered, which showed a high fixed right diaphragm with thickening of the adjacent lung field. The patient was also experiencing some difficulty in deep breathing, with pain over the right lower thoracic cage. With these facts in mind, a subphrenic abscess was suspected. Exploration and needling by the extra peritoneal route failed to disclose any suppurative process. Ten days later, the temperature subsided.

Contrast this case with another very definite picture of subphrenic suppuration as illustrated by Figure 4. The very definite fluid level and gas bubble give unmistakable evidence of abscess.

Lilienthal[5] points out that one of the very important methods of making a diagnosis of subphrenic abscess is the production of pneumo-peritoneum followed by

forative appendicitis, peritonitis and pylephlebitis with a very high temperature for seven weeks, developed a subphrenic abscess. Believing the abscess to be pointing anteriorly, a transverse incision was made below the costal border on the right side. Exploration revealed a large, tender liver behind which in the right posterior space, pus was located. Drainage was instituted from this point to avoid further tissue contamination. While considerable pus escaped from this uphill drainage, perforation of the diaphragm occurred twelve days later, requiring pleural drainage. Incidentally, a pleuro-bronchial fistula existed in this patient; this was discovered in Dakinizing the empyema cavity. The patient finally recovered.

The treatment of subphrenic abscess is obviously surgical, with dependent drainage. As pointed out earlier in this discussion, all subphrenic infections do not lead to suppuration, therefore, constitutional support of the patient and watchful care are required to



Fig. 3. Showing a high fixed diaphragm on the right side, with thickening of the adjacent lung field, in a subphrenic infection.

guide the individual safely until either resolution has taken place or suppuration has occurred.

When the abscess forms, its position should be accurately determined, so that proper operative approach may be made. Ochsner (previously quoted) found that the most frequent site of localization of subphrenic abscess is the right posterior superior space; this was involved in 28.8 per cent of his collected series of cases and 60 per cent of his own cases.

Extra-peritoneal drainage is the method of choice to avoid contamination of uninvolved serous surfaces of the pleural and peritoneal cavities. The method of Ochsner (previously quoted) for drainage of the right posterior superior and right inferior subphrenic spaces is to be commended. Briefly, the method consists in making an incision along the line of the twelfth rib. A subperiosteal resection of the twelfth rib is then done. In order to avoid transversing the pleural cavity, a transverse incision is made in the bed of the twelfth rib, at the level of the spinous process of the first lumbar vertebra, exposing the diaphragm, which is incised, and bringing into view the perirenal tissue. By displacing the kidney downward, the infrahepatic space is palpated. If a right posterior space abscess is suspected, the peritoneum on the under surface of the diaphragm readily can be separated by finger dissection. When induration is encountered, preliminary needling will determine whether or not suppuration is present. In the presence of pus, the finger may be inserted into the abscess cavity and drainage instituted.

Abscesses located in the right anterior superior, the left anterior inferior and the left superior spaces, if attached to the parietal peritoneum, may be drained readily, extra-peritoneally, through the anterior abdominal wall. If such abscesses have not approached the surface, a two-stage operation should be considered by packing against the abscess wall awaiting adhesions, followed by a second operation for drainage.



Fig. 4A. Antero-posterior chest film, showing fluid level and gas bubble in a subphrenic abscess.



Fig. 4B. Lateral view, same subject.

The right and left anterior space abscesses above the liver may be drained by the method suggested by Clairmont,[7] the incision being made along the costal border dividing the aponeurosis and separating the muscle layers until the parietal peritoneum is reached. The peritoneum is separated from the diaphragm and the exploring finger inserted into the abscess cavity, thus establishing extra-peritoneal drainage.

SUMMARY

Septic complications of intra-abdominal infection may be avoided in many instances by early operative treatment. It is estimated that perforative appendicitis is responsible for over 50 per cent of such complications.

After the infection has escaped from its local confines, conservative management, particularly in the presence of overwhelming toxemia, is indicated until localization occurs.

In the presence of abscess, early extra-peritoneal drainage should be instituted to avoid contamination of uninvolved serous surfaces.

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ABSTRACTS

PRIESTLEY, JAMES T., AND WALTERS, WALTMAN.

Indications for Operating in Gastric Syphilis. S., G. and O., Vol. LVIII, No. 6, June, 1934, 99:1030-1035.

In cases of gastric syphilis the symptoms are marked and progressive with an average duration of two years, and usually absence of an epigastric mass, retention, nausea, anaemia, cachexia and bleeding. This condition usually occurs during the second to the fourth decades of life, while gastric carcinoma from which it is to be differentiated usually occurs late in life. In cases of gastric carcinoma the symptoms are of shorter duration, and are accompanied by marked anaemia, cachexia and a palpable mass in the epigastrium. Roentgenologically gastric syphilis shows certain characteristics: there is a circumscribed or diffuse concentric involvement converting the affected segment into a narrow tube with a relatively smooth lumen of uniform caliber in which there is no intrusion of a distinct growth. There is some degree of stiffening, lessened mobility, and absence of peristalsis. The importance of an accurate differential diagnosis between gastric syphilis and gastric carcinoma is accentuated by the fact that treatment of the one is primarily medical, and of the other primarily surgical.

At the first examination cases in which there is serological evidence of syphilis associated with a definite gastric lesion may be classed in three main groups:

I. Cases in which the diagnosis of gastric syphilis can be established by all the clinical and roentgenological criteria outlined, and cases in which all the roentgenological and clinical evidences of an inoperable gastric lesion are present regardless of whether this appears to be syphilitic or malignant.

II. Cases in which serological evidence of syphilis is incidentally associated with an operable gastric tumor, or any gastric lesion in which medical care is insufficient.

III. Cases in which there is serological evidence of syphilis associated with a definite gastric lesion, the clinical diagnosis of which is indeterminate between malignancy and carcinoma.

In brief cases in Group I are usually primarily medical, whereas in Groups II and III exploration should be carried out. Those cases in Group I will be greatly benefited by medical treatment; surgical treatment is necessary when the lesion is obstructing, or when healing causes obstruction.

The authors believe that if antisyphilitic treatment will ultimately prove satisfactory definite improvement will be noted within two or three weeks.

Five illustrative cases in which operation was carried out are reported in detail.

Nelson M. Percy.

ORR, THOMAS G., AND CURPLEY, W. C.

Preoperative Preparation of the Dilated Stomach. S., G. and O., Vol. LIX, No. 1, July, 1934, pp. 92-98.

The authors state that in many cases of pyloric obstruction the stomach becomes markedly dilated and atonic. It hangs flaccidly in the abdomen like a bag filled with stagnant liquid, food particles and tenacious mucus. As a general rule it is unwise to operate upon any acutely distended portion of the intestinal tract because it probably will not heal normally, and restoration of function will be delayed and unsatisfactory.

A markedly dilated stomach after having been washed clean with a large stomach tube may be restored to normal size in an average from four to six days by using continuous gastric lavage with suction. An indwelling Levine tube passed through the nose is suitable for this purpose when connected with a suction apparatus.

During continuous lavage careful attention should be given to the maintenance of chemical, water, and metabolic balance. Glucose, chlorides and water may be given by vein, or by hypodermoclysis and proctoclysis.

The authors recommend that the blood chloride determination be made daily because the loss of chlorides by the gastric secretion greatly reduces the body chlorides which in turn upsets the whole metabolism.

The authors illustrate a modification of the apparatus employed by Ward, and later by Wangensteen.

Nelson M. Percy.

FLINT, E. R.

Sympathectomy in Megacolon and Constipation, from "Some Observations on the Sympathetic Nervous System." British Medical Journal, May 26, 1934, 942-44.

It is assumed that overaction of the sympathetic nerves or diminished action of the parasympathetic nerves is responsible for certain irregularities of bowel function, and in either case sympathectomy permits more effective peristaltic efforts of the colon. In Hirschsprung's disease no medical treatment alone is effective and hitherto, surgery has been too great a risk, but in sympathectomy we have a safe and undoubtedly efficient method of attack. The bowels act without enema, the abdominal distension decreases, the well-being improves and X-ray shows the appearance of haustration in the sac-like colon. The operation should be done in early childhood before the development of too much fibrous tissue in the hypertrophied wall of the colon. In spite of this operation there is a tendency to relapse, which only can be prevented by re-education of the bowel muscle under careful medical supervision. In cases of chronic constipation the operation should only be used in those cases which have failed to respond to all medical treatment. Cases which show absence of well-marked haustration, some distension and lengthening of the colon are the type suitable for operation. These signs show inhibition and such cases should respond to the operation. The reverse signs would show spasticity and presumably would not be improved by the operation.

The results of this operation on 16 patients, suffering the type of constipation described, may be considered very favorable. Fourteen of the cases have been followed and except for two who have relapsed into their former state, all show improvement. Six cases have daily bowel movements without any abdominal pain and are feeling very well. However, it is too early to draw definite conclusions as many of these cases have only been operated on in the last two years.

J. J. Day.

SECTION VII—*Surgery of the Lower Colon and the Rectum*

TREATMENT OF HEMORRHOIDS*

By

JEROME M. LYNCH, M.D., F.A.C.S.
and
VINCENT HURLEY, M.D., F.R.C.S.
(Engld.)
NEW YORK CITY, NEW YORK

THE treatment of hemorrhoids involves a careful scrutiny of the general condition of the patient, and the local condition of the anus, anal canal, rectum and recto-sigmoid. Hepatic cirrhosis, tabes dorsalis, ulcerative colitis, rectal carcinoma and polyposis are among the conditions which must be excluded with certainty before curative measures can be contemplated. Given, then, the presence of hemorrhoids and the absence of the aforementioned contra-indications, it is of importance to know what the local pathological picture is, as this largely governs the type of treatment. The pectinate line is of supreme importance; injection, for instance, is never advisable distal to it.

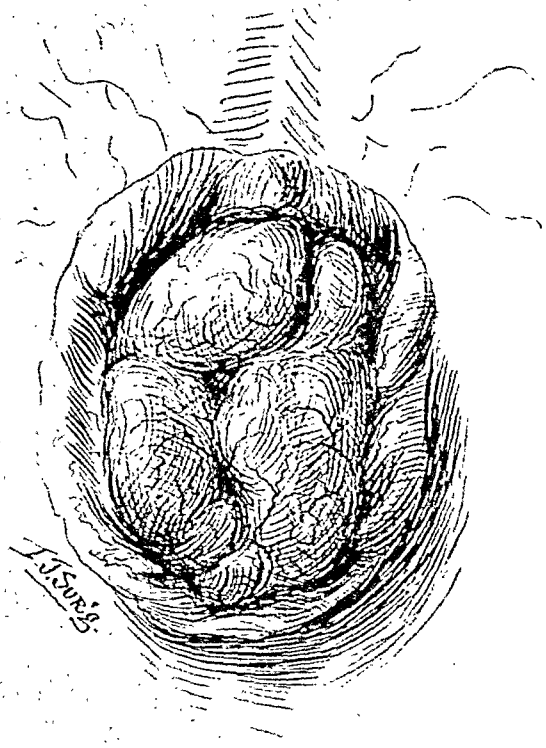


Fig. 1. Prolapsed Internal Hemorrhoids showing the three main positions where they develop.

External hemorrhoids are projections peripheral to the pectinate line and are of two types (1) the skin tag and (2) the subcutaneous clot or thrombotic hemorrhoid. *Internal hemorrhoids* are within (above) the pectinate line. They may be prolapsed at defecation to return spontaneously or be pushed back shortly after, or they may remain chronically prolapsed. (Fig. 1.) They are subject to thrombophlebitis and, in this state, may be prolapsed and become gangrenous. In addition, apart from what may be termed "inherent complications", fissure, abscess or fistula may be present as well as hypertrophied papillae and pedunculated, fibrous polyps. (Fig. 2.) It is clear, therefore, that no *one* therapeutic method will be of universal applicability; treatment must be planned for the individual case.

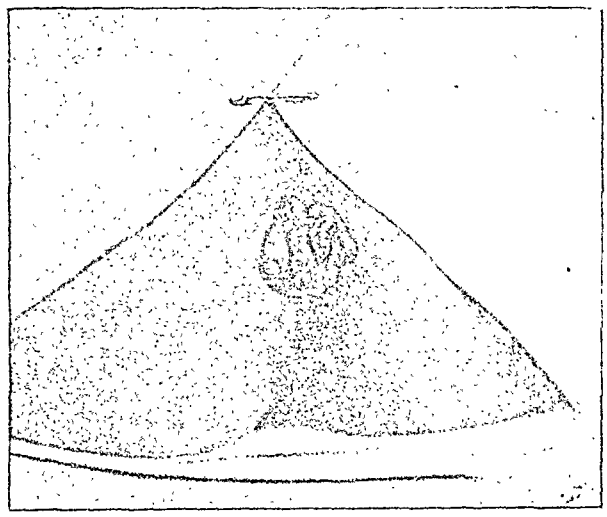


Fig. 2. Prolapsed Internal Hemorrhoids showing Hypertrophied and Inflamed Papillæ.

I. EXTERNAL HEMORRHOIDS

(1) Skin tags are satisfactorily treated by subjacent infiltration with novocain (1 per cent) and removal with scissors in such a manner that the wound is oval and radial to the anus. Small bleeding vessels are briefly compressed by forceps, a pressure dressing is applied and held firmly by a T-binder. The wound heals by granulation. If many tags are present there is a choice of removal at one sitting at the hospital or one at a time at weekly office visits.

(2) Thrombotic external pile or marginal subcutaneous clot is found usually at the right or left of the anus and rarely at the commisures. The etiology is somewhat obscure but a considerable percentage is associated with some type of effort. There are two varieties: the single, large clot which is extravascular (Fig. 3) and the cluster of small "bird shot" which may or may not be within the lumen of the veins.

*From the New York Polyclinic and Hospital, Surgical Clinic.
Submitted July 3, 1934.

Rarely, an external pile of this type is continued into a thrombosed internal hemorrhoid.

In the common, external variety under local anesthesia with novocain (1 per cent) an oval of skin corresponding in size with the lump—its long axis radial to the anus—is removed with the subjacent clot. In the bird-shot type, a similar oval of skin is excised and all the clots readily are removed with the help of pressure or are tied; packing the wound with a narrow gauze-strip, removed in 24 hours, gives excellent results also. A pressure-pad with firm T-binder is applied and is removed next day. The patient, usually a robust adult, continues at his occupation and merely

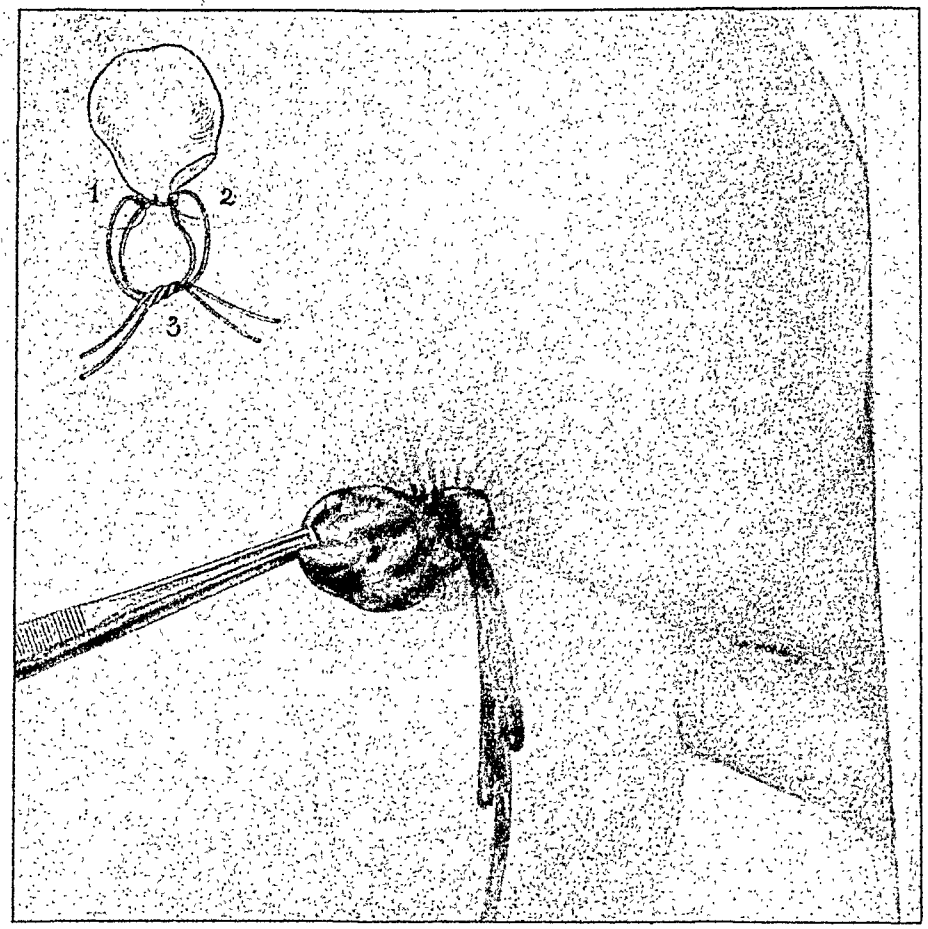


Fig. 3. Large External Thrombotic Hemorrhoids with Ulcerated Internal Hemorrhoid. Diagram in upper left corner, shows the ligature in place and method of tying.

requires supervision of the wound. The removal of an adequate oval of skin is followed by a linear scar and obviates the disagreeable tag following healing when other operative procedures are exhibited. In the rare cases where the external clot forms but a part of an interno-external thrombosed hemorrhoid which extends upward several centimetres from the anal margin, the operation will be of the type described below under the surgical treatment of internal hemorrhoids.

II. INTERNAL HEMORRHOIDS

(1) Injection. Uncomplicated internal hemorrhoids which manifest themselves by bleeding, by prolapse which is spontaneously or manually reduced or by bleeding and prolapse, are ideally suited to treatment by injection. It is unfortunately true that injection is a more delicate procedure than is hemorrhoidectomy and if improperly performed may be followed by disastrous consequences. Therefore, it is evident that those intending to practice the injection treatment should be well equipped with the necessary instruments and solutions and should have learned the technique from an expert in the procedure. Two injection solutions are in common use today: quinine and urea hydrochloride (5 per cent) in distilled water as first advocated by Terrell, and phenol (5 per cent) in almond oil, the modern form of the secret formula of the quacks of 70 years ago. Rarely, a 10 per cent phenol solution in almond oil will be required. These solutions, properly exhibited, will give results gratifying alike to the patients and to the surgeon.

The necessary equipment is simple: an anal speculum of any type to which the operator is accustomed, a 5 c.c. capacity syringe with a 10 cm. needle of 22 bore, and a headlight or other satisfactory means of illumination. The short, Tuttle speculum with distal illumination is an instrument which has given us much satisfaction. The patient may be in the knee-chest or the Hanes position—both are suitable for injection. Two procedures are available: the immediate injection of the four quadrants *at one seance* and following the patient closely in the hospital, or the single injections, at intervals, until the hemorrhoidal area is all indurated. In our opinion the second method is preferable; if hospitalization and quick action are indicated, we favor surgical hemorrhoidectomy. If the quinine and urea solution is used, 0.5 to 1 c.c. should rarely be exceeded as an injection dose. The phenol solution may be given in much larger amounts—we have given

10 c.c. at one injection into an especially loose submucosa, with an excellent result. However, a better method is to observe the mucosa and when the network of small vesesls stands out clearly, enough has been injected; this is the "striation sign". Emphasis should be laid on the site and level of the injection: *it must always be in the submucosa proximal to the pectinate line and preferably at the highest point of the hemorrhoid.* Injection of the mucosa is recognized by a blanching around the needle; a slough is inevitable. Deep injection of the muscular wall is to be deprecated as it may be followed by severe pain and long-standing discomfort, especially if the sphincters are involved.

The first injection nearly always stops bleeding or prolapse and succeeding injections usually are without incident. A series of indurations can be palpated in ring-fashion well above the anal margin in properly performed injections; endoscopic examination will reveal the presence or absence of soft, redundant tissue. If there is no evident hemorrhoidal tissue and no symptoms, the patient should be dismissed with the instructions to return for a check-up in three months. The advantages of the injection method are the absence of pain, loss of time from business, treatment is carried out in the office and there is no "operation" in the lay sense of the term. The disadvantages are the possible occurrence of sloughing or severe hemorrhage. Slough certainly is avoided by the correct placement of the injected solution; by so doing, also hemorrhage is minimized as it does not occur in the absence of slough. We encountered one unusual complication: following a single, correctly-placed injection of 2 c.c. phenol (5 per cent in almond oil), there was a marked swelling of the rectum and recto-sigmoid accompanied by tenesmus, mild obstruction symptoms, slight pyrexia and moderate leucocytosis. There was no bleeding or discharge. Endoscopic examination showed a swollen, pale, glassy mucosa somewhat resembling "bullous edema" of the bladder as seen through the cystoscope. The condition subsided in a week and was followed by obliteration of the internal hemorrhoids.

Following injection therapy, recurrence has been noted in approximately 10 per cent of cases. However, in such circumstances, the injections can be repeated with hope of satisfactory results. "Paraffin tumors" and strictures have been reported; obviously, they are the results of unsuitable solutions and poorly performed injections. (Fig. 4.)

2. OPERATION

We employ the ligature operation, slightly modified, to the exclusion of all other methods. Any complications such as fissure, polyp or spastic hypertrophied sphincter can be dealt with at the time of the operation. As preparation, 2 oz. castor oil are taken 36 hours before operation and cleansing enemas are not used within 12 hours of operation. As anesthesia, we have used local infiltration with novocain (1 per cent), spinal block with 80 to 100 mgm. of novocain crystals dissolved in spinal fluid, and on rare occasions, gas, oxygen and ether at the patient's special request. We lean strongly to local infiltration or spinal anesthesia. Three positions will be found suitable, the ventral or De Page, the left Sim's or the lithotomy posture. Our preference is for the De Page position but, occasionally, a very stout patient with prominent buttocks and a deep anus will be most readily handled in the lithotomy position.

A typical operation is as follows: The patient is placed on his abdomen on the table, the headpiece is turned up so that both hands and forearms can rest against it, the hips are placed opposite the break in the table which is now manipulated so that the patient is "jack-knifed" to a degree consistent with comfort and adequate anal exposure. A broad strip of adhesive now is applied to each buttock starting four inches from the anus; traction is applied to the outer end and, when the anus is well in view, the adhesive is fastened to the table, thus providing fixed retraction throughout the entire operation. The perianal region, adhesive and anus now are well painted with any of the usual antiseptic solutions and the area draped. Slight traction with the fingers on the perianal region will allow the lowest portion of each hemorrhoid to be brought into view. A curved hemostat (Kelly clamp) is introduced into the anal canal, opened and placed astride each pile, in turn, but in such fashion that *no skin is caught when the clamp is closed.* Traction now is made on the clamps and the piles and the canal can be inspected. Any one clamp is now selected and raised *up* and *towards the midline;* the muco-cutaneous junction is thereby exposed and divided with scissors *transversely* over a distance corresponding to the breadth of the pile. The clamp now is taken in the operator's left hand and pulled *down* and *out* exposing its tip; a round-bodied, curved needle carrying a strong linen or silk thread, then transfixes the pile a short distance below the clamp-tip, the needle is removed and the thread is firmly tied proximally and then both ends are brought out, one on each side of the clamp and again tied, the ligature thus being made to lie in the raw area previously produced by scissors cut at the



Fig. 4. Fibroid Tumors of the Rectum following the injection treatment for hemorrhoids.

pectinate line (m.c. junction). The other piles are treated in a similar manner; the area is carefully inspected for any bleeding point, the clamps are removed separately and the ligated piles are permitted to drop back into the rectum. Occasionally a very large pile may be partially removed by scissors beyond the ligature, but an adequate stump is always left. External tags now are snipped off and any other conditions demanding attention are dealt with. A spastic, hypertrophied sphincter associated with fissure (Fig. 5) is treated by division by knife in the posterior commissure. Lastly, the index finger is passed through the rectum and allowed to remain over night. If spontaneous evacuation does not then occur, a simple enema is given through a catheter. Sitz baths may be employed with advantage from the third day on. The patient sits up in bed or chair usually on the third or fourth day and may leave the hospital 24 hours later. The ligatures usually come away 8 to 10 days after operation and without pain. At this time, a digital examination is made so that the surgeon may be certain no "diaphragm" has formed. The olive oil instillations gradually are diminished and finally omitted. Four weeks after operation, the anus and anal canal present

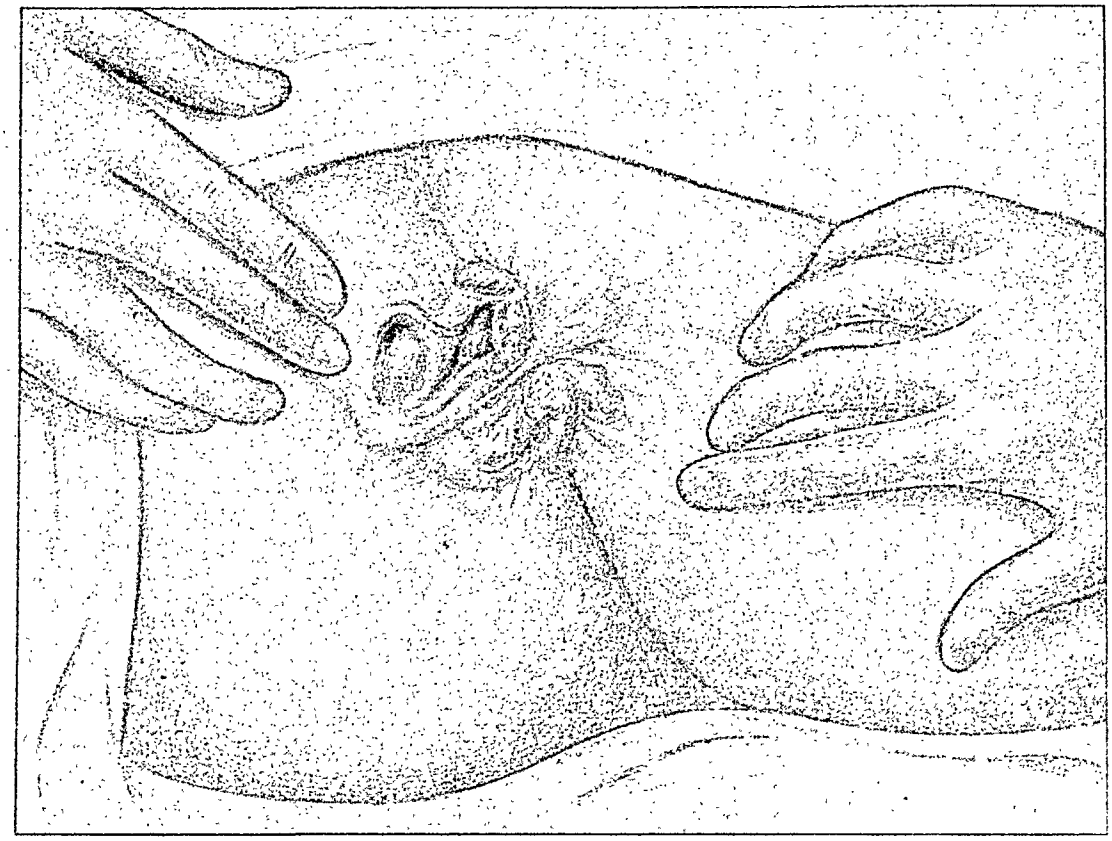


Fig. 5. Hemorrhoids complicated by Fissure.

canal to make sure that no "diaphragm" was made during the operation. Dressings are applied to the anus and perianal region in the form of an inverted pyramid; small pads over anus, covered by pads of gradually increasing size. The adhesive straps are removed and a large pad and T-binder firmly applied. Following operation, a sedative may be required for sleep on the first night but rarely thereafter. The need for morphine is unusual. As soon after the operation as desired, the patient chooses his own diet and no attempt at restriction is made. Catheterization of the urinary bladder may be necessary in some patients for the first urination but rarely thereafter.

After-care is of the simplest. Usually the dressing is changed after 48 hours and following each bowel movement. If there is unusual delay in moving the bowels, several ounces of warm olive oil are placed in a normal appearance; evidences of operation are minimal or absent.

It will be noticed that in the method outlined above, the sphincter is not stretched, the mucosa is not dissected up or stitched, there is a minimal amount of ligation of bleeding points, external tags are separately dealt with, skin wounds are not sutured, no special instruments are used and no tubes, plugs or drains are placed in the anal canal. Recurrences are uncommon: in our experience, less than one per cent.

SUMMARY

External hemorrhoids are treated by surgical removal when symptoms warrant.

Internal hemorrhoids, in the absence of complications, may be treated by injection or surgical removal; when complications are present surgery alone is indicated.

PERI-RECTAL STREPTOCOCCAL CELLULITIS*

REPORT OF A CASE

By

HERBERT T. HAYES, M.D., F.A.C.S.
HOUSTON, TEXAS

CASE *History:* Mrs. B. D. White, age 40, was admitted to the Memorial Hospital on February 2, 1934, complaining of hemorrhoids. Patient stated that she had had hemorrhoids for about twenty years and that they had given her great annoyance. They bled profusely, prolapsed badly with each stool and frequently induced severe attacks of pain. At intervals she ran a little afternoon temperature.

General examination was essentially negative, urine analysis normal; the blood count exhibited a slight secondary type of anemia. Rectal examination revealed very large prolapsing, ulcerated hemorrhoids.

The patient was *operated upon* February 3, under spinal anesthesia (50 mgs. of novocain) by the ligature and excision method. One-half per cent "diothane" was injected around the sphincter. The night following the operation the temperature was 103 degrees. Nothing abnormal could be seen about the rectum.

February 4, patient had a *chill* and her *fever* stayed around 102 degrees and on February 5, went to 104 degrees. At this time, there was definite induration on both sides of the rectum, not so marked posteriorly. On February 6, patient continued with chills and fever and on this date, she was given a gas anesthetic and the hardened area on both sides of the rectum was incised freely but no pus was exuded. On the right side, however, there was a serosanguineous discharge.

The peri-anal induration extended about two inches laterally and almost the same distance posteriorly, but was not marked in the perineal body. It also extended for about two inches up in the wall of the rectum. The mucosa of the rectum appeared normal. Cultures were taken from the base of the wound on each side by Dr. Myers.

The patient's temperature continued high during the next day, February 7, at which date the laboratory report showed a pure culture of streptococci. On the advice of the roentgenologist, Dr. Leonard Myers, treatment with X-rays was begun. The temperature dropped to 101.6 degrees within twelve hours after the first X-ray treatment. In less than eighteen hours, the wounds on both sides of the anus were draining a grayish-white, serosanguineous material very profusely. Subjectively the patient felt much better. On the next day and the day following she was given further X-ray treatments. During this time the wound drained profusely and the areas around the rectum softened rapidly.

The following dosage of X-rays was given:

2-7-34: Spark gap, 5 in.; M. amperes 3; no filters; distance, 10 in.; time, 3 min.

2-8-34: Spark gap, 5 in.; M. amperes 3; no filters; distance, 10 in.; time, 3 min.

2-9-34: Spark gap, 5 in.; M. amperes 3; no filters; distance, 10 in.; time, 3 min.

On the night of the 9th, patient's temperature became normal and did not go above 99 degrees after this time. Subjectively she was well; the hardness about the rectum had disappeared entirely. The sinuses gradually dried up; there was no communication with the rectum, no resultant fistulae and only one small, draining sinus when she left the hospital on February 20. A culture of the discharge from the wound, ten days after cessation of the X-ray treatments, proved it to be entirely sterile.

COMMENT: Due to the rarity of this condition as a complication of rectal operations, the literature available at the Library of The American College of Surgeons was reviewed; nothing of like nature could be found. The Transactions of the American Proctologic Society contained no cases similar to that being discussed. A review of the literature of the New York Academy of Medicine revealed three such postoperative complications. Dr. H. Smith of Kings' College Hospital, in reporting over 500 hemorrhoidectomies in 1875 and in 1878, stated that he had observed two patients who developed erysipelas of the rectum, postoperatively. One of these patients was extremely, almost fatally ill. L. Stein, Germany, in 1896, reported that, in 300 cases operated for hemorrhoids, he noted but one case of erysipelas. Pruitt, Gant, Lynch and others mention the fact that erysipelas of the rectum occasionally occurs but describe no specific case. Other authors mention the fact that streptococci often are found around the rectum, especially in instances of pruritus and that their presence is a potential danger in rectal operations, but report no instances of the organism's actually causing postoperative damage.

In the case here reported, the streptococci evidently were in the perirectal tissues and were carried into the wound at the operation by trauma or by the needle. This, apparently, accounted for the localized cellulitis.

While I was familiar with the use of X-rays in the treatment of erysipelas, I should not have considered employing it but for the suggestion of the roentgenologist. He predicted before the treatment that such therapy would have a very striking effect should it prove beneficial at all, that the inflammation immediately would begin to subside and a fistula would not follow. However, I was extremely dubious because the patient was so extremely ill. Not having had personal experience, I was unable to see how this prompt benefit could be predicted. It is to be noted that the patient's improvement began immediately after the first treatment and that subsequent treatments accelerated the beneficial results so that the patient became entirely well within a few days.

It is surprising that infections around the rectum are not more common. Apparently the local immunity of the tissues in this region is a protective barrier.

Caution: It should be emphasized that roentgen therapy to the perianal zone, whether for postoperative infection or for the treatment of *pruritis ani*, should never be exhibited subsequent to the application of oils, ointments or grease-containing suppositories. If X-ray treatments are given in the presence of such medicaments, very serious, extensive, tissue sloughs may follow, often with startling rapidity.

*Read before the Annual Session of the American Proctologic Association, Cleveland, Ohio, June 11-12, 1934.
Submitted July 22, 1934.

ABSTRACTS

FITZWILLIAMS, D. C. L.

Carcinoma of the Rectum. Lancet, 226, April 21, 1934. 842-44.

Carcinoma of the rectum comprises more than one-third of all cases cancer of the digestive tract. Although the commonest age incidence is between 50 and 60 years of age, it is important to note that 11 per cent of cases occur under 30 years of age. Pathologically it is an adenocarcinoma starting in the glands of Lieberkuhn. It may be one of three types, either the papilloma or cauliflower variety where growth is at a maximum and destruction is at a minimum, or the adenoid or common type where growth is at a minimum and destruction is at a maximum, as the growth spreads as a shallow ulcer with a hard edge, or the rare colloid form which is a degenerate form of the other two. The growth tends to spread around the bowel and penetration of the *muscularis* is slow. The veins of the bowel are important as it is by this means that the carcinoma reaches the liver.

There are no symptoms early. The first are slight constipation or frequent bowel movements without much passed. If the growth is low down there is incomplete relief from a bowel movement and the patient thinks he has piles. Blood is sometimes noted. Later the symptoms of chronic incomplete obstruction supervene and the usual picture of carcinomatosis develops. Fistulae between rectum, bladder or vagina are common and it is only by colostomy that these may be prevented.

Diagnosis is made by the history, examination of the abdomen, testing the stool for blood, etc., and most important, the digital examination of the rectum and lastly the barium enema and sigmoidoscope. Intussusception of a simple papillomatous growth or diverticulitis are the only conditions which might confuse the diagnosis and these are easily distinguished with careful examination. Colostomy with careful search of the entire abdomen for secondary growths is the first step in the treatment. Later, resection of the colon if there are no secondary growths. Radium may be installed in the distal part of the colostomy. J. J. Day.

FRADKIN, W. Z.

A Sigmoid Aspirator, J.A.M.A., 102:1381, April 28, 1934.

The sigmoid aspirator was devised to facilitate the obtaining of rectal and sigmoid contents in patients suffering from intestinal disorders. It is said to offer the following advantages:

1. The specimen is collected rapidly with simplicity and cleanliness.
2. The stool specimen is obtained in a fresh and warm state.
3. The instrument makes possible the collection of a stool specimen through a sterile field and into a sterile tube for transportation to the laboratory.
4. "Sterile" washings of the intestinal mucous membrane are easily obtainable.
5. The specimen is collected at the physician's convenience.
6. It avoids outside contamination.
7. The simplicity of the technic will make stool examinations by the physician a common rather than a rare occurrence and thus lead to a more scientific approach to the so-called nonspecific gastro-intestinal disorders. Samuel Morrison.

LOCKHART-MUMMERY, J. P.

The causation and treatment of multiple adenomatosis of the colon. Ann. Surg., 49:178-184. Jan., 1934.

This curious and rare disease has received considerable attention in recent years, due partly to the difficulty in finding satisfactory treatment and partly to the marked tendency to secondary carcinomatous change, resulting in death at an early age. The only treatment that seems to have any chance of success is early complete colectomy, followed by local removal of the tumors in the rectum at six monthly intervals. With this treatment, patients can live for long periods free from symptoms and protected from developing cancer. Cases watched for a considerable time show that absence of the colon does not prevent satisfactory nutrition, as none of the patients exhibited any permanent loss of weight. Slight looseness of the bowels is present in all of them, but not sufficient to cause serious inconvenience.

It can be definitely asserted that adenomatosis of the colon is an example of *gene* mutation, inherited as a Mendelian dominant, for excessive proliferation of the epithelium of the colon at about the age of puberty. O. L. F.

HANKINS, F. S., AND HARDING, W. G.

Acanthoma of Anus. Arch. of Surgery, 29-1-77 (July, 1934).

In a study of 1,097 cases of malignant tumors occurring in 9,000 consecutive autopsies at the Los Angeles County General Hospital there were three cases of epidermoid carcinoma of the ano-rectal region. This constituted an incidence of 1 per cent of all primary neoplasms of the gastro-intestinal tract and approximately 3 per cent of the carcinomas arising in the large bowel. Lynch's incidence of epidermoid cancer was 3 per cent of 491 cases, Pack's, 3 to 4 per cent. He reviews 40 cases ano-rectal acanthoma from the literature. Each of his own three patients had an associated syphilitic infection evidenced by positive Wassermann and Kahn tests with blood serum. He concludes that this type of growth is a low grade of malignancy. This is the prevailing opinion. Each of his three cases had a Grade 1 (Broders) malignancy. Early cases of a small growth may be treated by excision, preferably with cautery. When the growth is Grade 3 or 4, surgery should not ordinarily be resorted to. Here radium is indicated. Clement L. Martin.

BERRY, FRANK G.

Perianal Tuberculosis. Ann. of Surg., 99-4-593 (April, 1934).

The author reports 18 proved cases of tuberculous fistula from a Belleview Hospital surgical service. He mentions Chisholm's (1928) questionnaire to a number of Colorado physicians, seeking their opinion of operation for tuberculous fistula. It was: (1) Do you recommend operation? Only 2 favored it, 22 did not, 4 recommended it in selected cases; (2) Apparent end results? Twenty-four stated these were unfavorable, 41 favorable; (3) Anaesthetic employed? General 28, Local 0; (4) Technic: Knife 28, Cautery 0.

Berry's conclusions are that tuberculous fistula is not so frequent as is commonly supposed, that probably not over 5 to 10 per cent are tuberculous. That there is, however, a causal relationship between fistula and tuberculosis, in that the incidence of tuberculous fistula is higher in sanitaria for the tuberculous than in the general hospital. That in active pulmonary cases probably 75 per cent or more are tuberculous; in arrested cases probably only 15 to 20 per cent are tuberculous. That perianal tuberculosis is rarely if ever a primary lesion, so the original focus should be sought elsewhere in the body. Berry reported 72 per cent of cures in his cases operated upon.

Clement L. Martin.

MCLANAHAN, S., AND STONE, HARVEY B.

Enterogenous Cysts. S. G. and O., 58-6-1027 (June, 1934).

The authors report two cases of enterogenous cysts associated with the rectum. The case histories are given; one patient was a woman of 48 years, the other a one-month-old boy. The majority of previously reported cases were of cysts in the ileo-cecal region.

In their own cases the cyst lining was definitely enteric. In their discussion the work of Evans, who emphasized the great preponderance of intestinal diverticula in early life, and Lewis and Thyng, who 25 years ago demonstrated the epithelial origin of these diverticula in the pig, rabbit and human embryos, is cited. The origin of enterogenous cysts is thought to be in these small diverticula and so it becomes easy to understand that such cysts and diverticula may in reality be different phases of the same process; thus it is not difficult to explain on the above basis the location of a cyst in the intestinal wall, be it submucosal, intermuscular or subserous. In addition, the tumor may lie at any point in the gut periphery, anti-mesenteric, mesenteric, or at an intermediate site. Many lie between the folds of the mesentery. Clement L. Martin.

BLOOM, DAVID.

Strictures of the Rectum Due to Lymphogranuloma Inguinale. S. G. & O., LVIII, 827-839, May, 1934.

Bloom reports seven cases of rectal stricture under his observation in 1932-33, three of whom were males, four were negroes. All gave a positive Frei test and were "greatly benefited" in general health and local rectal conditions by tartar emetic or gold injections. The author, from a review of the clinical descriptions of "esthromene" and "syphilome ano-rectal" by Fournier, Jersild and others on one hand and the earlier reports concerning "benign inflammatory stricture" from Buie, Hayes and others, concludes that these conditions are identical and are due to the virus of lymphograpoloma inguinale. Curtice Rosser.

SECTION VIII—*Editorial*

The editorial contributions published in this Journal represent only the opinions of their writers. Such being the case, this Journal is in no way responsible for editorial expressions.

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

THE AFFILIATION OF THE JOURNAL WITH THE AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION

For many years the American Gastro-Enterological Association has felt the desirability and the need of having an American journal whose columns would be exclusively devoted to the publication of investigative medical and surgical articles dealing with Diseases of Digestion.

Such a journal should be planned to meet the requirements of clinical and research investigation into the etiology, the life history or course and the treatment of such diseases in their various aspects.

When the American Journal of Digestive Diseases and Nutrition was launched in 1934 and had presented its March, April and May issues, they were of such high caliber as to attract the favorable interest of our Association. As a result, at its annual 1934 session, our voting membership passed a resolution recommending and empowering our Executive Council to make overtures toward securing this Journal as the "Official Journal" of our Association.

After several months of negotiation, this affiliation has been completed, with the understanding that the editorial policy shall be under the joint control of the American Gastro-Enterological Association, the Editors, and of the Editorial Council of the American Journal of Digestive Diseases.

Hereafter, as long as this affiliation is mutually satisfactory, all papers and addresses presented before the American Gastro-Enterological Association at its Annual Meeting will be published in this Journal. This, we have reason to believe, will be of great advantage, not only to our own members, but to all students of gastroenterology and metabolism, whether internists, surgeons, roentgenologists, physiologists, pathologists, biochemists, research or laboratory workers.

How valuable it will be to have the great majority of the best papers published in one journal, instead of being scattered throughout a dozen or more!

Because the Editorial Council of this Journal includes nine members from Canada and eighty-four members from various sections of the United States whose ability in this subject is well recognized; because the abstracted literature of gastroenterology from domestic and foreign sources is and will continue to be an important feature of this Journal, and, above all, because we are assured that this Journal will continue to be published, editorially and otherwise, in accordance with the high standard of medical ethics as prescribed and practiced by the American Medical Association and by the better American societies of medicine, we are proud to acknowledge it as the "Official Journal" of the American Gastro-Enterological Association.

Other domestic and international journals of gastroenterology have heretofore sporadically appeared for brief periods and "died aborning", but we predict that this Journal will have a brilliant future so long as it continues to maintain its high standard of editorial supervision of accepted manuscripts and other subject matter and thus will serve to fill a much needed void.

If this is accomplished, it will certainly enhance the value of American medical literature. Whenever it ceases to do so, the American Gastro-Enterological Association will withdraw its support and seek elsewhere.

B. B. Vincent Lyon, Philadelphia,
President of the American Gastro-Enterological Association.

THE JOURNAL, ITS READERS AND THE AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION

With this issue The American Journal of Digestive Diseases and Nutrition becomes the "Official Publication of The American Gastro-Enterological Association".

The assumption of such affiliation was not made without mature deliberation on the parts of both the Association and the owners and Editorial management of The Journal. Apart from the consideration of many minor advantages which might accrue to the Association or to this Journal from joining forces, in the end, the factor in the affiliation which carried the greatest weight with the Journal's management was, "Would the union result in this Journal's becoming of greater practical worth and usefulness to the general reader—the practitioner who is busily engaged in practicing internal medicine, and who, perhaps, on account of natural ability or a liking for solving problems in, or managing patients with, digestive or nutritional disorders, has accumulated a considerable following in the specialty?"

The balancing of "pros" and "cons" in the situation finally convinced The Journal's management that the reader who is not a member of The American Gastro-Enterological Association nor concerned with its policies would secure quite as much benefit—probably more than—from our affiliation with that organization as would its Fellows and Associate Fellows.

The American Gastro-Enterological Association was founded nearly thirty-eight years ago as a society of specialists in the investigation, diagnosis and management of ailments affecting the digestive tract. Its membership is limited to one hundred "Active" Fellows and twenty-five "Associate" Fellows. In addition, there is a small group composed of "Research" Fellows and another of "Emeritus" Fellows—the latter made up of men who have passed the age limit set for Active Fellowship. All members are elected to Fellowship on the basis of ethical practice, community and institutional standing and affiliations and of work done, investigative or clinical, in the elucidation or treatment of alimentary tract disorders. During its more than thirty-seven years of existence, The American Gastro-Enterological Association not only has included in its

Roster this country's and Canada's leading research scholars and clinicians—surgical as well as medical—but has maintained a solid position as the outstanding organization in its field on the Western Hemisphere. The Association's Annual Meetings—they have been held uninterruptedly since its foundation—have become a distinguished forum for the presentation of authoritative work in investigation and practice. These annual sessions have attracted an increasingly large attendance of practitioners and experimentalists who are members of other organizations but who do not care to miss the contributions brought to the annual sessions or the stimulation which comes from the presentation of new work or the free discussion of that work by those best capable of discussing it.

The Association regularly has issued the Proceedings of its Annual Sessions in the form of "Transactions". These bound Volumes now form the archives of practically all progress made in gastroenterology during the past thirty-seven years. Their indices carry the names and the studies of nearly all our most esteemed investigators and clinicians. To one sufficiently fortunate to possess a complete set of the "Transactions" there is a mine of rich and practical literature available. Perusing these Volumes often demonstrates that not a few modern "researches"—purely scientific or clinical—amply were covered by men who, long since, have passed on. Complete sets of the "Transactions" are "out of print" but occasionally, by communicating with the Association's Recorder, Dr. Sara Jordan, Boston, one may pick up the bound "Transactions" for at least the past ten years. Even so limited a number of Volumes forms a real addition to the library of anyone whose major interests lie in gastroenterology and nutrition.

Not only will The American Journal of Digestive Diseases and Nutrition publish the papers and the discussions of the annual meetings of The American Gastro-Enterological Association but arrangements have been completed whereby, under the auspices of the Journal, the Annual "Transactions" will be issued, attractively and substantially bound in cloth. Such volumes will be available to the general reader at a low price.

In order to facilitate the relationship of this Journal with The American Gastro-Enterological Association, the President of the Association, Dr. B. B. Vincent Lyon, Philadelphia, has appointed the following Committees:

Co-ordination Committee

Dr. Thomas R. Brown
Dr. Richard H. M. Hardisty
Dr. Noble Wiley Jones
Dr. Frank H. Lahey
Dr. Howard F. Shattuck
Dr. Sidney K. Simon
Dr. B. B. Vincent Lyon *(Chairman, Ex-officio).*

Publication Committee

Dr. Leon Bloch
Dr. Geo. B. Eusterman
Dr. Andrew C. Ivy
Dr. Abraham H. Aaron
Dr. A. J. Carlson
Dr. B. B. Vincent Lyon *(Chairman, Ex-officio).*

It will be the function of these Committees not alone to forward the interests of the Journal's readers by the securing of representative manuscripts for its columns but by aiding the Journal in its maintenance of the high standard for material printed already set by the Journal's management. Such co-operation should assure present as well as prospective subscribers that the funds which are expended in these economically strenuous times will not be wasted: no other journal in a special field should be able to return to the subscriber greater value in investigative effort and in practical knowledge. Already, plans have been made which will insure this Journal's being a necessity to practitioners who wish to have available the exact knowledge which research alone can supply and the practical methods of diagnosis and management which can come only from clinicians who, day by day, are in touch with great groups of patients and whose efforts are checked by institutional records.

It will be of interest to readers to learn that there will be no increase in the annual subscription rate as a consequence of the Journal's affiliation with The American Gastro-Enterological Association; indeed, the Journal's management is looking forward to the day when a greatly increased subscription roll will allow a reduction in the present subscription fee.

From the standpoints of increased usefulness and a wider range from which worth-while contributions to its columns will be possible, the Journal congratulates its readers upon its affiliation with The American Gastro-Enterological Association. It is with due modesty that the Journal regards its having been selected by the Association as its "official publication". The Association, too, doubtless feels happy that the affiliation consummated offers opportunities for the wider spread of its influence in circumstances which are more than ordinarily favorable. Certainly, those representatives of the Association who carried forward the transaction to so successful an outcome deserve the plaudits not alone of their fellow-members but of all interested in a literature which will better represent what really is being accomplished in diseases of digestion and nutrition on the Western Hemisphere. Personally, the Editor, a former President of the Association and one who, for nearly twenty years, has been vitally and sympathetically interested in its standing and achievements, finds a source of much pleasure in the consummation of plans, long cherished, whereby the Association is to have its "official" publication and American medicine, through such publication, will have available a really representative special literature.

F.S.

SECTION X—*After "Hours"*

"ASTROLOGICAL PHYSICK"

By

CLEMENT L. MARTIN, M.D.*
CHICAGO, ILLINOIS

A short time ago an interesting book, *Astrological Physick*, came into my hands. It is a small thick volume of about 800 pages with spotted and worn covers but with all its pages intact and generally in an excellent state of preservation. It was published in 1671, little more than two hundred years after Gutenberg started to use his press at Strassburg and was written by Dr. William Salmon and dedicated to Dr. Peter Salmon of the Honourable Society of the College of Physicians of London. It is replete with quaint expressions. The work gives an interesting insight into medical practice, or at least one type of it, 263 years ago. The spelling is variable and punctuation is indifferent. Much emphasis is given to the astrological aspect of medicine and there is appended to the book, tables of Declination and Right Ascension and a set of logarithms so the doctor of the day could be assured in prescribing his medication under the proper auspices. One had to be something of a mathematician in order to prescribe in that day.

CLASSIFICATION OF MEDICINE

It is interesting to note the classification of the various agents used. Among others are the following:

"*Emollient Medicaments* are such as soften and reduce a hardness to an equal temperature": or thus, an "*Emollient* is that which by heat and moisture warms what is congealed and moistens its dryness."

"*Relaxers* are such as loosen any member distended through cold, dryness or repletion of wind, humours, or other matter, and they are a little hot and very moist."

"*Rarifying Medicines* are such as being of thin and subtle parts make tough and thick humours thin and rare and so fit them for expulsion being only so hot as neither to draw matter together nor yet to discuss it being gathered."

"*Attenuating Medicines* are such as by a gentle cutting quality loosen the bowels and open up obstruction there."

"*Attractives* are such as by their heat and thinness draw humours and matter to any part of the body desired."

"*Repercussives, Repulsives,* or *Repellers,* are such as by a cold quality, being astringent, also drive back the matter or humour to some other place."

"*Discussives* are such as generally disperse the matter and so dissolve it inseparably."

"*Anodynes* are such as by a gentle warming or temperate quality ease and take away pain without having regard to cause or anything else."

"*Narcoticks* are such as by their exceedingly cold quality ease pain by stupefaction or dulling the senses."

"*Suppuratives* are such as by a natural heat bring blood, raw superfluous and undigested humors (*sic,* sometimes spelled with the u, sometimes without) to matter and ripeness."

"*Incarnatives* are such things as breed flesh, changing the blood thereinto."

"*Pectorals* are such medicines as are appropriated to the breast and lungs."

"*Cordials* are such medicines as are appropriated to the heart and these cheer, comfort and revive the spirits."

"*Ptarmica* are medicines which purge the brain by sneezing. These by their attractive qualities draw the Flem into the nostrils, which hangs about the pellicles of the brain and by their acrimony provoke the expulsive faculty and cast it out with such excrement as sticks in the brain itself."

In Chapter 58, *On Diseases of the Lower Ventricle or Belly* the author describes "*colicus dolor;* the cholick if it be gentle and the belly soluble, it is easily cured; but if great, fixed and the belly bound, with watching, vomiting, hiccough, cold sweats and coldness of the extream parts, it is deadly; if it come of Cholerick Humours it sometimes degenerates into the Palsie, Falling Sickness, or Gout."

Among other diseases noted are:

"*Melancholia Hypochondriaca* with continued pain and giddiness of the head gives fears of the Epilepsie, Apoplexie, or Blindness; if accompanied by a moderate flux of the belly, vomiting or the haemorrhoids, it is good; this disease is generally long and seldom cured." Many gastro-enterologists will confirm this last statement.

The prevailing notions in regard to cancer may be inferred, in part at least, from the following: "*Schirrus,* if it comes once to have no feeling, it is incurable; in all other cases it is very difficult. If it suppurates it degenerates into a cancer; but in the beginning while it is little there may be hopes of resolution."

"*Cancer* if it happen in the stomach, paps, head, shoulder, neck, or under the arms, it is generally incurable because these parts are dangerous to be cut, for the great flux of blood which may ensue. If it happen in the nose it is called *noli me tangere;* if in the legs or thighs, Lupus a wolf, but in other parts it is called cancer."

"*Lumbrici,* worms in the beginning of the disease (are) to be avoided as most deadly whether they be alive or dead for it is by great putrefaction that they are sent out."

*Clinical Professor of Proctology, Loyola University, School of Medicine, Chicago; Chief of the Proctologic Clinic, Mercy Hospital, Chicago.
Submitted July 30, 1934.

"*Icterus,* the Jaundice, happening in a feaver before the crisis, is dangerous, and contrariwise if on a critical day; if it comes upon an inflammation of the liver it ends in an imposthume (abscess); if upon a Schirrus it ends in a dropsie; upon obstruction of the gall it is curable."

"*Rheumatismus,* distillation of rheum to the joynts or running gout; in old age or in asthma is incurable."

"*Arthritis,* the gout, if it be knotted in the joynts or in extream age is said to be incurable."

"*Cholera,* if its original be from evil food when the sharp matter is cast forth it will end; if very violent with convulsions, swoundings, or coldness of the extream parts, death is at hand."

The psychiatrists and brain surgeons might be interested in this: "if the brain be affected; before you strengthen it purge it and when you purge it let it be done with cephalics; and before you purge it let the whole body be cleansed lest it soon be filled with vapours again.

DRUGS

Four hundred and three different agents are listed. The virtues claimed for some of them are remarkable. With so many drugs for the common diseases the physician had a wide choice. Apparently the old principle that many remedies for a disease meant that none was of certain value held true. The few drugs described below will convey an idea of this section of the book.

"*Hepatica,* liverwort, it opens the liver, spleen and gall, cures tertians, jaundies, rickets."

"*Herniaria,* millegrame, rupture-wort, it cures ruptures, the jaundies, fluxes and gonorrhea."

"*Lactuca,* lettice, it stops fluxes, gonorrheoas, helps spitting blood, cures ruptures" (thus perhaps the persistence of the belief in its sedative effect; "lactucarium U.S.P., an extract of lettuce juice has been used considerably as a narcotic but no basis for this employment has ever been discovered in scientific experiments. Tyrode 1908.)

"*Lavendula,* lavender, it cures the palsie, convulsions, falling-sickness, swounding, cholick, dysentaria, stranguria, kills worms, expels melancholly, comforts and strengthens the heart, nerves, liver and spleen."

"*Psyllium,* fleawort, applied with vinegar, it helps swellings in the joynts, it purges choller, and is good for dysentarias and corrosion of the guts."

Tithmalum (plant of the euphorbia species) is highly recommended as a cathartic thus: "the seed or leaves purge choller, flegm and water violently; give six or twelve seeds or four or five leaves at a time. Outwardly it blisters and takes off hair."

The advocated *treatment of hemorrhoids* follows: "To stop the flux of them the Essence of Mars (a preparation of iron) is good given inwardly and also the conserve of roses with fine bole. *Crocus Metallorum,* (a powder of yellow oxide of iron) applied to the piles abates pain and consumes the swelling. Excellent is the ashes of cork with capon's grease, oyntment of toad flax or pile-wort, as also a girdle of green leaves of black hellebore bruised and tyed about the naked body applying to them opium dissolved and mixed with the yolk of an egg or saccarum saturni (a "salt" of red lead) with butter. If they swell much bleed with leeches, then anoynt with an oyntment made of white cucumber."

The *Decoctum Traumaticum* was highly recommended for all sorts of sores and wounds. The prescription is:

"℞ Prunella	Mii (2 handfuls)
Angelica, Sanicle, Betony, Rosemary, Sage, Red Beets, Scordium, Agrimony, Soapwort, Plantain, Comfry, Hypericon, Cinquefoil, Mint, Oats, Oak, Daisie Leaves, ā	Mi (1 handful)
Guaiac, Anniseeds, ā	oz 1ss
Ale or Wort	15 qts."

"Rasp the wood and roots and bruise the herbs and boil all together to the wasting of about two quarts and when almost cold put yest to it in a roundlet and after four days drink constantly of it.

"It takes away all manner of pain and soreness of wounds and drives out and casts out all manner of filth, splinters and pieces of bones and then heals in a few days. It cures all fistulas, inward and outward sores, stancheth inward bleeding and cures the king's evil to admiration."

Among the *unusual and curious medicaments* are:

"*Oleum Bufonum Hartmani,* or Oyl of Toads of Hartman, R. (Take) 3 or 4 living toads, boyl them a whole hour in oyl olive ii lb. and keep it for use. This oyl is a wonderful virtue against pimples, morphew, freckles, sunburning, wheals and redness of the skin or face: anoynt the skin or face once a day for certain days, after a little time the wheals will fall off and the morphew or redness disappear."

"*Oleum Catellorum* or oil of whelps R., oyl olive or oyl of lillies lb. iv, in which boyle two whelps, newly whelped, earthworms cleansed or washed in spirit of wine lb. i, boyl all until the flesh of the whelps parts from the bones and then strain all hard and put to the oyl, venice turpentine, oz. iv, spirit of wine oz. i mingle them, S.A. It is a wonderful force to assuage pain, to help old bruises and aches and bring gunshot wounds to suppuration and to cause the eschar to fall off."

"*Unguentum Sympatheticum* or sympathetic oyntment R., boar's grease, brains of a boar, powder of washed earthworms, red sanders, mummy, bloodstone, a., oz. i, moss of a dead man's skull not buried, dr. i, make an oyntment, S.A. All wounds are cured by this oyntment (provided the nerves and the arteries be not hurt) thus: anoynt the weapon that made the wound, daily once, if there be need and the wound great otherwise it will be sufficient to anoynt it every other day. Where note, (1) that the weapon must be kept in clean linen and in a temperate heat lest the patient be hurt; for if the dust fall or the wind blow upon it or it be cold the sick will be much tormented; (2) that if it be a stab the weapon be anoynted towards the point descending; (3) if you want the weapon, take blood from the wound upon a stick and use as if it were the weapon; thus the toothache is cured by pricking the gums or anoynting the instrument."

And so men practiced and prescribed when Louis XIV was in his glory in France, when Charles II reigned in England, and so they lived and so they died while Milton dreamed his dreams and put them into imperishable verse.

Astrological Physick came into my hands through the kindness of Dr. Wm. E. Morgan, now 76 years old, in practice more than half a century, one of C. H. Mayo's teachers at the Chicago Medical School in the eighties and on the staff of Mercy Hospital with John B. Murphy. His own medical career has seen changes in the practice of medicine comparable with the difference between the practice of today and that described in *Astrological Physick.* A grateful patient, D. Fadalia Sadaliski, a Polish Count, presented the book to Dr. Morgan.

CORRESPONDENCE

(From time to time the Journal will publish in some form the more interesting cases which come to its attention via correspondence. Answers to questions raised will be furnished by Council members, although it is not imperative that either the name of correspondent or Council member be given.)

Q. A woman, æt. 49, complains of constant burning in the right side of the mouth, especially the lower jaw and tongue, and nothing prescribed so far has done any good.—B. P.

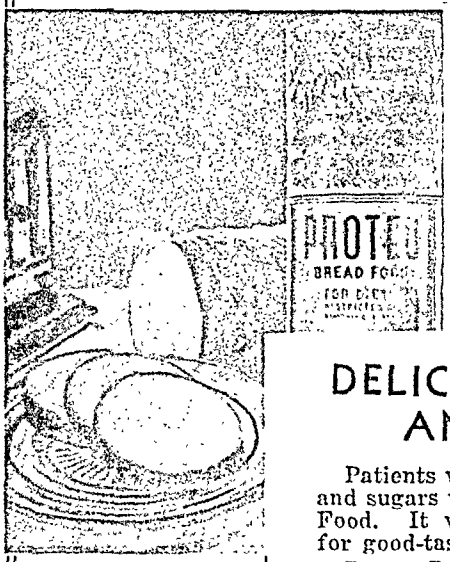
A. The details of the case as set forth in your letter show that the burning sensation came on 18 months ago, following extraction of teeth in the lower jaw, also that she has "hot flashes" and other symptoms pointing to the vaso-motor instability of the menopause. Gastric analysis indicates a normal acid secretion, and for this reason, as well as because the mouth is not symmetrically affected, one does not think of the glossitis of pernicious anemia. Apparently she has no marginal redness of the tongue; and one cannot make out any mucous membrane lesions of any kind; and the X-ray films of the edentulous jaws, as well as of the antrums appear quite normal. Probably you are dealing with a mild trigeminal irritation, resembling tic, although actual pain is not present. This results from the trauma of dental extraction in one whose reaction type is decidedly hypersensitive and almost pathological. General measures, such as rest, freedom from responsibility, physiotherapy, well balanced diet, and careful psychotherapy in the attempt to divert attention from the abnormal sensation, will probably do more good than local measures, although many of these "atypical facial neuralgias" are the bugbear of the neurologists.

Q. A man, æt. 52, presented a tense, painful swelling of the lower portion of the right parotid gland, becoming gradually more painful over a period of two weeks. What to do?

A. Your examination was limited apparently to the region affected, but you have given all the information required for a presumptive diagnosis of parotitis. A complete set of dental films revealed no evidence of apical infection, and clinically the teeth which remained were in fair condition. An X-ray of the mandible showed normal bone. Films of the floor of the mouth and a picture taken through the right antrum, with the film held against the roof of the mouth, showed no evidence of calculi in the salivary ducts. It is suggestive that the leucocyte count has been around 18,000 per c. mm. during the last few days, with 88 to 90 per cent polymorphonuclears and 1 to 2 per cent of basophiles. He is afebrile, which so often is the case in parotitis. When occurring in association with abdominal operations, parotitis carries a high mortality. Probably early incision in this case would be advisable. A guarded prognosis should be given.

Q. A woman, æt. 47, has complained for two years of weight loss progressively from 199 to 100

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(Ca=.21, P=.36, Fe=.005)		
Cellulose substances, Pentosans, etc. (by difference)	6.	—
Crude Fiber	1.	—

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at the present time, although no definite diagnosis has seemed possible. Management?

A. Your data are extremely exhaustive, and sufficient to rule out much chance of an organic background such as syphilis (although a spinal tap might be done), diabetes, hyperthyroidism or cancer. The vomiting would be more alarming if it were not for the fact that this woman has always been a vomiter. She probably did overwork (as a housemaid) for the past few years. Again, the stress seems to fall chiefly upon her extreme anorexia, which was periodically, but only temporarily, overcome by tube feeding. The weight loss appears to parallel the meager caloric intake. From the expression of her face in the photograph, one would suspect a good deal of mental degeneracy. *Anorexia nervosa*, certainly always but a symptom, seems here related to the mental condition. The bad effects of anorexia nervosa often lend it the aspects of a real disease and one extremely difficult to treat successfully. Some of these patients fall prey eventually, in their weakened state, to some fatal acute illness such as pneumonia, while others to some chronic disease such as urinary infection, against which they seem to have very little resistance. Frankly most cases prove obdurate to any kind of treatment. Occasionally, a change of scene works marvels. Some of these unfortunate degenerates suddenly take a "new interest" and eat and recover for no recognizable reason. One patient, the victim of protracted anorexia, overheard relatives planning how her property was to be divided after her death, and her dramatic recovery was definitely related to a sudden desire to live and "show them."

Q. Do you consider that pyorrhea alveolaris and apical dental infection constitute focal infection of importance in dealing with digestive diseases?—B. E. McL.

A. Yes. Quite apart from all arguments regarding the "elective affinity" of micro-organisms for various tissues (which has reasonable supporters and perhaps equally reasonable opponents), the fact remains that most patients improved *from a general standpoint* following sane treatment of pyorrhea or the sane irradication of apical infection. The improvement in general tonus is often enough to help them overcome digestive symptoms, especially where these are of a functional nature. In the case of organic diseases, such as chronic biliary infection or peptic ulcer, such good results occur but rather as the exception. Irradication of mouth infection is nevertheless advisable, provided care and judgment are used in the surgical procedures. I do not know of any definite proof that dental infection causes peptic ulcer or cholecystitis, but the partial causative role seems obviously possible and even likely. Great harm may result from massive dental extraction of infected teeth—pulmonary abscess, septicemia, and also the ill effects on nutrition in persons unable to adjust to artificial dentures. I thoroughly believe that you are always justified in accurately diagnosing the mouth conditions in gastrointestinal cases, but fortunately the day is almost past when the physician advises indiscriminate dental extraction.

Q. What is the best treatment for mucous colitis?—G. A. S.

A. This is a perfectly legitimate question, but the answer must be made with endless provisos and individualizations. Buckstein's recent book on the treatment of functional disorders of the large intestine could be consulted with benefit. The smooth diet is nearly always, as you suggest, a prime desideratum, and yet, occasionally, malnourished individuals actually do better in the long run, to eat "what they want." Sedatives are of value if not pushed to the point of causing or increasing mental depression. Belladonna is widely used, but many internists have discarded it because of its frequent idiosyncratic effects. Soricin, and other similar products, are gaining in favor, although perhaps the *modus operandi* is not very clear. The extreme instances of mucous colitis are cases to overtax the efforts of the best physicians. Many cases are truly incurable. In some we suspect the emotional or mental life as being responsible indirectly for the symptoms. One caution is to be emphasized—the most complete and painstaking examinations are necessary, for you will find cases of amebiasis who for years have paraded as mucous colitis. No case should be so labeled until every possible effort has been made to place them in some other category.

THE VITAMINS

Vitamin A was first called "fat soluble A" by McCollum, and was shown to be essential to the continued growth of animals, since animals only fed pure food substances soon ceased to grow, but quickly resumed growth when fed additionally those substances which contained vitamin A, particularly butter fat, egg-yolk fat, kidney fat and cod-liver oil. In 1913, Osborne and Mendel observed a severe inflammation of the eyes in a number of animals after several weeks' deprivation of vitamin A, a condition quickly cured by the administration of foods containing the vitamin. This condition is due to a lack of tear secretion. Xerophthalmia in the human subject has been frequently encountered, notably during the World War in Roumania, and was cured by cod-liver oil, which is rich in A. Night blindness in India is cured by feeding liver. A mass of evidence has been collected to show that vitamin A is effective in assisting the body in its fight against infection. The treatment of pneumonia and post-puerperal infections by this vitamin has given encouraging results by reducing mortality. Vitamin A, if taken in large quantities, is stored in the liver and hence an animal or human individual may withstand deprivation for several weeks. Successful child-bearing requires a sufficiency of vitamin A in the food. A color test for the detection of vitamin A is used. The substance is standardized by the method of Sherman, using rats which have been deprived of A to the point of growth cessation: the amount of the vitamin which, when added to the deficient diet, permits a growth of three grams a week is the "vitamin unit." The richest source of vitamin A are the fish liver oils, especially cod or halibut, but the leafy parts of plants are good sources also. The natural foodstuff richest in vitamin A is the green vegetable escarole, belonging to the endive family. *Excellent* sources are also butter, cream, spinach, carrots, dried whole milk, and cheeses made from whole milk. *Good* sources are prunes, peas, raw and canned tomatoes, evaporated and condensed milks, bananas, broccoli, yellow corn, Brussels sprouts,

cantaloupes, dried green peas, sweet potatoes, dates, artichokes, and whole cow's milk. Leaf lettuce is a good source, but head lettuce is only a fair source. Vitamin A is heat-resistant, except in the presence of a current of air, when rapid destruction takes place. Canning usually does not impair the A content of food substances. Carotene (or carotin), the yellow plant pigment of carrots, is really *provitamin A*, and has the simple chemical formula, $C^{40}H^{56}$. This provitamin, when eaten, is taken to the liver, where it is changed to vitamin A by the addition of oxygen. The commercial concentrates are derived from carrots, one being known as carotene. It is now known that the continued use of mineral oil causes a complete loss to the body of vitamin A, because carotene is also a hydrocarbon and the oil takes it with it via the feces.

Vitamin B (B1) was first called "water soluble B" by McCollum, because it is soluble in dilute alcohol in water. It is, of course, the lack of this vitamin which causes beri-beri in man, and polyneuritis in pigeons, both of which are susceptible to cure by the administration of B1 in sufficient amounts. Like A, B1 promotes growth, and it is also important as being the appetite-promoting vitamin. Appetite is lost in B1 deprivation, because the stomach muscles become atonic and hunger contractions are no longer possible. Vitamin B permits the body to subsist normally on a greatly reduced general ration, by increasing absorption. Animals deprived of vitamin B show a great reduction in the amount of stored glycogen in the liver.

By 1926 it became apparent that the "vitamin B complex" was really a dual force, because, although prolonged heating destroyed the antineuritic factor, it did not damage the growth-promoting factor. Human pellagra, the black-tongue of dogs were benefited markedly by the administration of cooked yeast, from which, of course, all antineuritic influence was removed. A pellagra-like condition was then produced in rats by feeding vitamin B only, and cured by giving them cooked yeast. This quality of vitamin B becomes clear if we remember that it contains (1) vitamin B1, the anti-neuritic and growth-promoting factor, and (2) vitamin B2, the pellagra-preventing factor. This latter is often referred to as vitamin G. Cow's milk, while containing appreciable amounts of vitamin B2, is deficient in vitamin B1 for growth as well as for lactation. Brewers yeast and wheat germ are the two most prolific sources of vitamin B. Rice polishings and some types of bakers yeast are excellent sources. *Good* sources are spinach, carrots, tomatoes, and lettuce. The whole grain cereals are also potent in vitamin B, but not dependable because of their being consumed in bread in the degerminated form. Oranges, prunes, cantaloupes, nuts, liver and kidney are good sources also. While ordinary cooking temperatures have little effect on vitamin B, it is very unstable at higher temperatures, especially in an alkaline medium. The canning of tomatoes, pineapples, peaches and carrots does not impair their B content, and the evaporation and drying of milk loses only 20 percent of B1 and none of B2. Probably the average American dietary is quite deficient in vitamin B, which finds expression in anorexia, digestive disturbance and certain types of malnutrition. The real reason for this is the milling of wheat whereby all the B1, B2, A, E, as well as most of the minerals, go to the cattle. Fortunately some firms are now including sufficient wheat germ in all their flours to obviate this defect, present since 1879. While we do not see in our American practices true infantile beri-beri such as is common in the tropics, many of the dyspepsias of babes and children are unquestionably due to the low ebb of vitamin B in the average diet. Sure succeeded in producing a very potent B preparation from rice polishings. Most of the commercial concentrates are made from wheat embryo. It is still questionable if vitamin B has ever as yet been isolated in an absolutely pure form, although some crystalline concentrates have been obtained.

Vitamin C prevents and cures scurvy, a disease caused by the lack of fresh fruits or vegetables. All practitioners are familiar with acute infantile scurvy, which responds so dramatically to the juices of citrus fruits. Only the guinea pig can be used to determine the distribution of vitamin C, as it is the only cheap animal that develops anything closely resembling human scurvy. Spinach and peppers are the most potent anti-scorbutics: then come raw cabbage, tomatoes, citrus fruits, parsley, raw peas. The citrus fruits are so potent and dependable that orange juice has become a universal routine in infant feeding. Strained juice of canned tomatoes is a good alternative. The potato is only a fair source of C, but it is so popular a food that it has a definite anti-scorbutic influence, and scurvy always appears following failure of a potato crop. Vitamin C is the most unstable of all in cooking, even in home cooking. The presence of copper, and an alkaline medium hasten the destruction. Dental caries may be an expression of scurvy; raw seal meat contains C, as Stefansson cured scurvy with it. Strangely enough, vitamin C is a very simple substance, namely, hexuronic acid, but there are 16 different kinds of hexuronic acids, and the exact identification of the formula C(6)H(8)O(6) has not been made.

Vitamin D is the dietary factor which prevents and cures rickets, a disease of the bones. Although cod-liver oil has been in use for two centuries and longer, its em-



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ployment as a cure for rickets is of recent date. As late as 1918, a prominent pharmacologist wrote that "it (cod-liver oil) taken repeatedly, increases the weight and strength . . . the same good effects are obtained in healthy persons by the use of good foods and fats." In 1922, McCollum showed that 1 percent cod-liver oil was superior to 20 percent butter fat in curing rickets caused by low calcium diet. This was shown later to be due to the presence of a distinct antirachitic vitamin in cod-liver oil which was not vitamin A. The best source of vitamin D is haliver oil, which is 25 times as potent as medicinal cod-liver oil and has the added advantage of being 100 to 125 times as potent in vitamin A. Egg yolk is an excellent source of D. Oysters are very rich in the antirachitic vitamin. These two foods are the only ones which are rich sources of D; hence we see that our natural diet is extremely low in this substance. Fortunately, however, sunshine is a substitute. Ordinary cooking has no effect on vitamin D. The irradiation by the mercury quartz vapor lamp of certain foodstuffs, such as olive oil, gives them definite antirachitic properties, and this applies also to spinach, carrots, wheat flour, butter, milk, and breakfast foods. Ergosterol, when irradiated sufficiently, may become 1,000,000 times as potent in D as the average cod-liver oil. Ergosterol was then thought to be "provitamin D," and, although D has been isolated as a crystal, the real isolation of pure D remains still to be accomplished. Animals can be killed by overdosage with viosterol. The latter is not a substitute for cod-liver oil, as it contains no A. The convenience of haliver oil becomes apparent, as it supersedes cod-liver oil in both factors. A hen will lay regularly if given D as cod-liver oil or as sunlight or as mercury quartz vapor lamp, but viosterol has no such effect. Fish probably have the power to synthesize vitamin D. When sunlight or mercury quartz lamp light penetrates the skin, it activates the ergosterol of the subcutaneous tissues and produces viosterol there. Vitamin D in the body acts as a regulator of the calcium-phosphorus metabolism. D cures not only rickets but osteomalacia, and infantile tetany. No reports have been seen of its effect on the adult tetany, either strumipriva or the gastrointestinal type.

Vitamin E is the food factor whose absence causes sterility in both male and female, and the administration of which to animals so deficient cures the sterility in the case of females, but not of males. Wheat germ oil is the best source, although it occurs also in cottonseed oil, corn oil and palm oil. Peach kernel, soybean, peanut and olive oils are potent for curing sterility, but are nonpotent for lactation. Egg yolk is a very rich source of E. Among vegetables the best sources are lettuce, spinach, alfalfa, and water-cress. Skeletal muscle and fat contain much more than liver. Vitamin E is not destroyed by cooking, unless when mixed with fats that become rancid. It is not yet definitely proved that human sterility due to lack of E occurs, but some reports of good results in cases of habitual abortion are suggestive. (Abstracted from The Vitamins in Health and Disease, by Barnett Sure, Williams and Wilkins, Baltimore.)

READERS PLEASE NOTE

The September issue of the American Journal of Digestive Diseases and Nutrition will be devoted exclusively to the Transactions of the American Gastro-Enterological Association, and will present not only an exceptionally fine collection of original contributions, but what frequently is of even greater interest and of equal value, pointed discussions of these papers by members of the Association. The September issue will, therefore, be larger in pages than usual and the customary format and sectional divisions will be discarded for convenience and simplicity.

Back numbers of the Journal are mostly exhausted with exception of those held back for volume binding. Physicians eager to obtain back numbers may advertise with success in the pages of this Journal.

Original Articles In Previous Numbers

VOLUME I

CLINICAL MEDICINE:

AMEBIASIS AND AMEBIC DYSENTERY—*Chas. F. Craig, M.D., M.A., F.A.C.S., F.A.C.P.*

AMERIC DYSENTERY IN CHICAGO—*Herman N. Bundeson, M.D., Sc.D.*

CERTAIN LATENT AND ATYPICAL TYPES OF AMEBIASIS—*Philip W. Brown, M.D.*

MIGRAINE, AN ALLERGIC PHENOMENON—*Albert F. R. Andresen, M.D., F.A.C.P.*

DIAGNOSIS AND MANAGEMENT OF GALL TRACT, PARTICULARLY GALL BLADDER, DISEASE—*B. B. Vincent Lyon, M.D., A.B., Sc.D.*

GASTRIC ULCERS ASSOCIATED WITH CINCOPHEN POISONING—*Leon Bloch, M.D., and David H. Rosenberg, M.D.*

OBSTRUCTION OF THE UPPER PORTION OF THE SMALL INTESTINE—*Andrew B. Rivers, M.D., and Norman W. Thiessen.*

THE BROADENING CONCEPTION OF REGIONAL ILEITIS—*Burrill B. Crohn, M.D.*

FOOD ALLERGY IN ITS RELATION TO GASTROINTESTINAL DISORDERS—*Julius Friedenwald, M.D., and Samuel Morrison, M.D.*

REPORT OF AN INSTANCE OF SUPPURATIVE CHOLANGO-HEPATITIS WITH OBSTRUCTIVE JAUNDICE—*B. B. Vincent Lyon, M.D., Damon P. Pfeiffer, M.D., and John Eiman, M.D.*

OBSERVATIONS UPON AMEBIASIS—*Virgil E. Simpson, A.B., M.D., F.A.C.P.*

JAUNDICE WITH ASCITES—*William Fitch Cheney, M.D.*

CHRONIC ULCERATIVE ENTERITIS—*Philip Corr, M.D., and William C. Boeck, M.D., F.A.C.P.*

GASTRIC SECRETION FOLLOWING IRRADIATION OF THE EXPOSED STOMACH AND THE UPPER ABDOMINAL VISCERA BY ROENTGEN RAYS—*Albert M. Snell, M.D., and Jesse L. Bollman, M.D.*

SINGLE GASTRIC POLYP—REPORT OF AN INSTANCE—*Martin C. Vorhaus, M.D., and Arthur E. T. Rogers.*

RECURRENT HIATUS HERNIA SYNDROME OF VON BERGMANN—*Felix Cunha, M.D.*

THE RESULTS OF TREATMENT—MEDICAL AND SURGICAL—IN GALL BLADDER DISEASE—FROM A CLINICIAN'S VIEWPOINT—*Thomas R. Brown, M.D.*

LATE MANIFESTATIONS OF AMEBIASIS—*R. W. Mendelson, M.D.*

COMPLEMENT FIXATION TEST FOR AMEBIASIS (PRELIMINARY REPORT)—*Emil Weiss, M.D., and Lloyd Arnold, M.D.*

LAMBLIASIS SIMULATING CHOLELITHIASIS—REPORT OF TWO INSTANCES—*Meyer Golob, M.D.*

BRILLIANT BLUE F.C.F., A NEW DYE FOR DIAGNOSTIC GASTRO-INTESTINAL STUDIES—*Arthur C. Taylor, M.D.*

THE OCCURRENCE OF A PERNICIOUS ANEMIA SYNDROME IN THE PRESENCE OF NORMAL GASTRIC ACIDITY—REPORT OF AN INSTANCE—*A. L. Levin, M.D.*

HISTORY OF GALL BLADDER DISEASE—RESUME OF SYMPTOMS—*Martin E. Rehfuss, M.D.*

A PRACTICAL ETIOLOGICAL, PATHOLOGICAL AND CLINICAL CONSIDERATION OF INTESTINAL ULCERATION—*Joseph Felsen. M.D.*

INSANITY EQUIVALENTS AND THE GASTRO-ENTEROLOGIST—*Walter C. Alvarez, M.D.*

INTRAVENOUS GALACTOSE LIVER FUNCTION TEST—PRELIMINARY REPORT—*I. R. Jankelson, M.D., and H. H. Lerner, M.D.*

UNUSUAL CLINICAL SYNDROMES ASSOCIATED WITH STONE IN THE COMMON BILE DUCT—*Albert M. Snell, M.D., and Manfred W. Comfort, M.D.*

EXPERIMENTAL PHYSIOLOGY:

SYMPATHETIC SECRETORY INNERVATION OF THE GASTRIC MUCOSA—*Stewart G. Baxter, M.D.*

ROLE OF THE SYMPATHETIC NERVOUS SYSTEM IN GASTRIC SECRETION—*Stewart G. Baxter, M.D.*

THE RELATION OF GASTRECTOMY TO ANEMIA—*A. C. Ivy, Ph.D., M.D., O. Richter, M.D., A. F. Meyer, Ph.D., and H. Greengard, M.S.*

GASTROINTESTINAL STUDIES: IV. THE RELATION OF pH TO THE PEPSIN AND RENNIN CONTENT OF THE GASTRIC JUICE—*O. M. Helmer, Ph.D., Paul J. Fouts, M.D., and L. G. Zerfas, M.D.*

AN INVESTIGATION CONCERNING CERTAIN SUBSTANCES REPORTED TO AFFECT THE MOTILITY OF THE GALL BLADDER—*W. L. Voegtlin, M.D., and A. C. Ivy, M.D.*

THE ANTIPEPTIC INFLUENCE OF GASTRIC MUCIN—*Earl A. Zaus, M.D., and Leonard S. Fosdick, Ph.D.*

THE INFLUENCE OF THE PYLORUS UPON THE REGULATION OF THE ACIDITY OF THE GASTRIC SECRETION—*William Walsh Lermann, M.D., and Lyle M. Nelson, Jr., M.D.*

THE COMPOSITION OF PURE GASTRIC JUICE—*Franklin Hollander, Ph.D.*

RECENT INVESTIGATIONS PERMITTING A NEW INTERPRETATION OF THE RESULTS OF THE CONVENTIONAL TITRATION OF GASTRIC JUICE—*Lay Martin, M.D.*

DISSOCIATION OF THE FUNCTIONAL PROPERTIES OF THE GASTRIC GLANDS UNDER THE INFLUENCE OF FAT—*Armine Alley, M.A., David W. MacKenzie, Jr., B.A., and D. R. Webster, M.D., Ph.D.*

NUTRITION:

NUTRITION IN HEALTH AND DISEASE—*Clifford J. Barborka, B.S., M.S., Sc.D., M.D.*

LOWER FAT DIET IN DIABETES—*Joseph H. Barach, M.D.*

ESTIMATION OF THE STATE OF HYDRATION OF THE BODY BY THE AMOUNT OF WATER AVAILABLE FOR THE SOLUTION OF SODIUM THIOCYANATE—*Lathan A. Crandall, Jr., M.D., and Milford X. Anderson, M.D.*

THE DIETARY PHASES OF PERNICIOUS ANEMIA—*Beaumont S. Cornell. M.D., F.A.C.P.*

MORTALITY IN DIABETIC CHILDREN—*Henry J. John, M.D.*

THE EFFECT ON THE GASTRIC JUICE SECRETION OF VARIOUS COOKED PREPARATIONS OF HADDOCK (MELANOGRAMMUS AEGLEFINUS) AND OF LOBSTER (HOMARUS AMERICANUS)—*A. Alley, M.D.*

A STUDY OF OBESITY IN AN OUTPATIENT CLINIC—*Edgar C. Beck, M.D., and Roger Hubbard, Ph.D.*

THE INCIDENCE AND SIGNIFICANCE OF DISEASE OF THE GALL BLADDER AND LIVER IN PERNICIOUS ANEMIA—*Frank H. Bethell, M.D., and Bernard D. Harrington, M.D.*

ROENTGENOLOGY:

WHY PEPTIC ULCERS ARE MISSED ON X-RAY EXAMINATION—*Wm. H. Stewart, M.D., and H. Earl Illick, M.D.*

CHOLECYSTOCOLIC FISTULA WITH X-RAY DEMONSTRATION—Martin G. *Vorhaus, M.D., and Arthur E. T. Rogers, M.D.*

X-RAY'S CONTRIBUTION TO THE DIAGNOSIS OF THE "ACUTE ABDOMEN"—*Wm. H. Stewart, M.D., and H. Earl Illick, M.D.*

FACTORS OF ERROR IN ROENTGENOLOGIC DISTINCTION BETWEEN THE NORMAL AND THE DISEASED STOMACH AND DUODENUM—*B. R. Kirklin, M.D.*

INTENSIFIED ORAL CHOLECYSTOGRAPHY—PRELIMINARY REPORT—*William H. Stewart, M.D., and H. Earl Illick, M.D.*

THERAPEUTICS:

TREATMENT OF AMEBIC DYSENTERY—*Horace W. Soper, M.D.*

INSULIN IN THE TREATMENT OF PEPTIC ULCER—*Clement R. Jones, M.D.*

CHRONIC ULCERATIVE COLITIS: TRENDS IN ITS PRESENT-DAY MANAGEMENT—*J. Arnold Bargen, M.D.*

TREATMENT OF PEPTIC ULCER WITH BACTERIAL VACCINES (FOREIGN PROTEIN)—*David J. Sandweiss, M.D., and S. G. Meyers, M.D.*

ABDOMINAL SURGERY:

PRIMARY CARCINOMA OF LIVER IN INFANCY—*Ralph A. Kordenat, M.D.*

TWO SPECIMENS OF GASTRIC AND DUODENAL ULCERS ANATOMICALLY CURED BY SURGERY—*L. Blagdon, M.D., and L. C. Simard, M.D.*

DIVERTICULOSIS AND DIVERTICULITIS OF THE SMALL INTESTINE—*Irvin Abell, M.D.*

THE CONGENITAL PERICOLIC MEMBRANE SYNDROME, OFTEN MISNAMED CHRONIC APPENDICITIS—A PRELIMINARY REPORT OF OBSERVATIONS—*W. H. Buecrmann, M.D., Ph.D.*

ACUTE LIVER DEGENERATION: TREATMENT BY CHOLECYSTOGASTROSTOMY WITH DISCUSSION OF THE CLINICAL, PATHOLOGICAL, AND PHYSIOLOGICAL ACCOMPANIMENTS—*Chas. Gordon Heyd, B.A., M.D., F.A.C.S.*

CONSERVATIVE SURGICAL TREATMENT OF ULCER OF THE STOMACH AND DUODENUM—*E. Starr Judd, M.D., and George W. Waldron, M.D.*

AN ANALYSIS OF THE RESULTS OF BILIARY TRACT SURGERY—*John Tilden Howard, M.D.*

THE TREATMENT OF CARCINOMA OF THE COLON—*W. Wayne Babcock, M. D., F.A.C.S.*

SURGERY OF THE LOWER COLON AND OF THE RECTUM:

UNUSUAL PROBLEMS IN THE PLASTIC SURGERY OF THE COLON—*Jerome M. Lynch, M.D., F.A.C.S., and Vincent Hurley, M.D., F.R.C.S.E.*

MULTIPLE FISSURES OF THE ANUS IN A CASE OF TERTIARY SYPHILIS—*Louis A. Buie, M.D., and Winfield L. Butsch, M.D.*

TUBERCULOUS ULCERATION OF THE RECTUM AND SIGMOID—*Clement L. Martin, M.D.*

DIAGNOSTIC CRITERIA OF RECTAL CANCER—*Curtice Rosser, M.D., F.A.C.S.*

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SECTION I—*Clinical Medicine: Diseases of Digestion*

A HISTOLOGIC STUDY OF THE LIVER IN PATIENTS AFFECTED WITH PEPTIC ULCER*

By

MAURICE A. SCHNITKER, M.D.

and

GEORGE M. HASS, M.D.

BOSTON, MASSACHUSETTS

MANY contributions to the etiology of peptic ulcer indicate that biliary and pancreatic secretions play a *rôle* in this disease. As the result of Boldyreff's (1) contention that regurgitation of these alkaline secretions serves to neutralize the acid gastric juice, numerous workers have attempted to prove that a failure of normal regurgitation is responsible for the development of peptic ulcer. A few writers, however, believe that the formation of an ulcer may depend upon the deficiency of some substance either in one or both of these secretions. Berg and Jobling (2) among others, have expressed the opinion that the mechanism by which the exclusion of bile predisposes the mucosa to ulceration probably depends on the loss of some constituent in the bile which is essential for the maintenance of an intact surface epithelium of the stomach and duodenum. These observers thought that this substance might be mucus. It seemed possible that a deficiency of some substance might be a better explanation of the clinical picture of ulcer than the theory which is based upon the concept of a failure of acid neutralization.

As no studies of the liver have been recorded in patients with peptic ulcer, a histologic investigation of this organ in one hundred *post mortem* cases of ulcer seemed to be sufficiently valuable to place upon record.

LITERATURE

A brief review of the literature shows that in many instances a disturbance of the liver or its secretions is followed by the development of a peptic ulcer. The more successful *surgical means* used to produce ulcers experimentally have been concerned either with the sidetracking or the shutting-off of the bile or the pancreatic juice, or both, from the duodenum. The historical development and types of operation have been presented most admirably by Alvarez (3).

One of the earliest experimental procedures was that of Bickel (4), who in 1909 removed the duodenum in two dogs, closed the pylorus and did a gastroenterostomy, bringing the biliary and pancreatic ducts out to the skin. One of the dogs died from a perforated ulcer. Moutier's experiments (5) in 1910, Langenskiöld's (6) and Kehrer's (7) in 1914 similarly resulted in ulcerous lesions, but the most successful chronic ulcers were produced by Mann and Williamson (8) in 1923 and Morton (9) in 1927 by diverting the biliary and pancreatic secretions into the lower bowel. This "surgical drainage of the duodenum" resulted in the formation of ulcers in from fifty to one hundred per cent of the animals. Kapsinow (10) in 1926 drained the contents of the gall bladder into the renal pelvis in forty-three dogs and seventeen of these developed duodenal ulcers. A high incidence of ulcers in dogs with Eck fistulae and biliary obstruction and following removal of part of the liver was noted by Bollmann and Mann (11) in 1927. Bollmann (12) and Bollmann and Mann (13) ligated and sectioned the common bile duct in dogs in an attempt to produce ascites and found that death in most of the animals was due to perforation of a peptic ulcer. The authors stated that the factors which influenced the formation of ulcers did not seem to be related to the duration of the resulting obstructive jaundice.

With a one-way valve in the jejunum or in the pylorus to prevent regurgitation of alkaline duodenal juices, Matthews and Dragstedt (14) in 1932 delayed the healing of artificially produced ulcers of the stomach. In a surgical study of the regenerative capacity of the extrahepatic biliary tracts, Halperin (15) noted that in nine dogs an incomplete stenosis of the common bile duct and a hepatitis developed. Seven of these nine dogs showed ulcers. In 1932, Schrager, Ivy and Morgan (16) introduced a new method for the plastic reconstruction of the common bile duct. They observed seven of the dogs for a long period of time. After three months all the dogs exhibited elevated icteric index although bile was present in the stools. Six of these had varying degrees of biliary cirrhosis and five developed duodenal or gastric ulcers (17). Hosomi (18) had made similar observations in 1928, lesions occurring in seven of fifteen dogs.

The pancreatic juice usually is more alkaline than is the bile; it has been considered to be the better buffer (3), although Jones (19) has shown that the two act in a compensatory manner. On the basis of the alkalinity of the pancreatic juice, various attempts have been made to produce ulcers by excluding only this secretion. According to the earlier workers, Minkowski (20) and others, the pancreatic duct may be ligated with no resultant damage to the intestine. Berg and Jobling (2) were unable to produce ulcers by sidetracking the pancreatic juice, but Ivy and Fauley (21) found duodenal ulcers in six of sixty-one

*From the Department of Medicine and the Department of Pathology of the Peter Bent Brigham Hospital, respectively, and the Harvard Medical School, Boston.

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dogs who had pancreatic fistulae. In four dogs with pancreatico-ureteral anastomoses, Loewy (22) observed no ulcerations after the prolonged loss of pancreatic juice over a period of from sixteen to thirty-seven days. Elman and Hartman (23) reported spontaneous ulcers in six dogs after the total loss of pancreatic juice for thirteen or more days, but the lesions were only defects in the continuity of the mucosa and did not involve the deeper muscle layers of the intestine. Berg and Zucker (24) and Berg (25) recently repeated these experiments with essentially negative results. One dog, which developed jaundice and marked degenerative changes in the liver, had perforating ulcers. These authors (26) have demonstrated previously that dogs with pancreatic fistulae subsequently develop cloudy swelling and fatty infiltration of liver cells which process progresses to necrosis, atrophy of liver cords and cirrhosis. These observations suggest the possibility that the lesions which follow the loss of pancreatic secretion may be the result of such secondary changes in the liver.

In addition to the production of ulcers by the alteration of gastro-intestinal physiology by surgical procedures, there are numerous reports of instances of the development of ulcers following the use of *chemicals*. Numbers of these have been effective, supposedly as a result of damaging the liver or by altering its secretion. The spontaneous development of ulcers in dogs has been reported, according to Ivy, Schrager and Morgan (17), by Quigley and Helm, following the administration of borneol, a camphor, and by Thomson after poisoning with salicylic acid. In these instances there was a hepatitis or a disturbance of liver function. By giving alcohol or lead by mouth and by an intestinal route, and by injecting *B. coli* into the gall bladder and biliary passages, Wichels, Brinck and Lauber (27) demonstrated changes in gastric function and secretion. The result was a cirrhotic change in the liver and the development of peptic ulcers. Van Wagoner and Churchill (28) fed massive doses of cinchophen which produced marked hepatic changes and the development of chronic peptic ulcers in nearly one hundred per cent of dogs. Churchill and Manshardt (29) have shown that these ulcers were not due to the local action of the drug upon the stomach.

From time to time isolated reports have occurred in the literature of patients with *peptic ulcer and liver disease*. In a review of two hundred cases of surgical lesions of the biliary tract by Sherwood (30) in 1928, twenty-nine cases (14.5 per cent) had associated gastric or duodenal ulcers. Shapiro and Lifvendahl's study (31) of fifteen cases of tumors of the extrahepatic ducts showed four to have a duodenal ulcer. Maluschew (32) reported two cases of hepatic *echinococcus* disease associated with gastric ulcer. Duodenal ulcer occurring with acute yellow atrophy of the liver also has been reported (33). Bloch and Rosenberg (34) reviewed two cases of cinchophen poisoning with associated gastric lesions but the lesions were not typical ulcers. Not only liver disease, but the association of cholecystitis with peptic ulcer has been mentioned frequently. Eusterman (35) stated that from thirteen to eighteen per cent of cases with chronic ulcer have an associated disease of the gall bladder. Rivers and Mason (36) found 13.6 per cent of patients with duodenal ulcer and 7.8 per cent of patients with gastric ulcer to have cholecystic disease. In the cases primarily diagnosed as cholecystitis and cholelithiasis, these authors found a peptic ulcer in 3.2 per cent, and Moynihan (37) found it in 7.4 per cent.

In spite of the not infrequent association of hepatic disturbance and peptic ulcer, there has been very little discussion in the literature about a possible relation between the two. Gundermann (38) in 1913 stated "that it is possible that ulcers are produced through a dysfunction of the liver." On the basis of Sellards' work (39), Tsuruta (40) suggested such a relationship. Ivy, Schrager and Morgan (17) mentioned the possibility of hepatic disorder associated with the occurrence of ulcer in man but their search of the literature failed to disclose any studies of the histology and function of the liver in patients who exhibited peptic ulcer. We have been able to find only one report, that by Vilardell and Llort (41) in 1932; these observers described a hepatitis occurring in four instances of gastric ulcer and three of gastric cancer. On the basis of this possible relationship, Berg and Jobling (2) produced biliary fistulae and biliary obstruction in a series of dogs and found that ulcers resulted in fifty-six per cent of their experiments. The animals showed varying degrees of changes in the liver.

In summary, there is much in the literature to suggest the possibility of an association between a disturbance of the liver or its secretions and the development of peptic ulcer, although there is nothing in this evidence which is conclusive. One must remember that experimental ulcers may be quite different from the disease as seen spontaneously developing in man, yet it is important enough that it should not be ignored. Recently, in this clinic, hemorrhage into the gastro-intestinal tract in a few cases of cirrhosis of the liver has been attributed to the rupture of esophageal varices. The disclosure of a bleeding peptic ulcer at necropsy in such patients has directed attention to the possible relationship between cirrhosis of the liver and peptic ulcer. At the present time, the evaluation of liver function tests seems too unsatisfactory to justify such procedure in studying any possible association. Therefore, it seemed that a histologic study of the liver in patients with peptic ulcer might return facts of significance.

MATERIAL

In making a study of this kind it was necessary first to consider the incidence of gastric and duodenal ulcers in patients who had cirrhosis of the liver. Secondly, it was essential to study the livers of those patients who came to autopsy and who were affected with a peptic ulcer. Thirdly, it seemed advisable to have a control series composed of cases which were not diagnosed primarily as having either cirrhosis or ulcer. The *post mortem* material in the Peter Bent Brigham Hospital, covering the eleven-year period, 1922-1933, was utilized for this study.

During this period there were seventy-two cases of advanced cirrhosis of the liver, of which fourteen (19.5 per cent) coincidentally exhibited peptic ulcer. There were one hundred instances of typical gastric or duodenal ulcer, and inasmuch as these were selected from the same eleven-year period as was the cirrhosis group, necessarily they included the fourteen cases of cirrhosis with ulcer. Combining the two groups, a total of one hundred fifty-eight cases was reviewed.

The *average age* at death of the one hundred fifty-eight patients was 54.29. The average age of the patients affected with cirrhosis alone was 53.22, and of the patients with ulcer alone, 55.36.

In the one hundred cases of typical ulcer, the gastric or the duodenal lesion presented various stages of pathologic development. The ulcer was located in the stomach in thirty-six patients on an histopathologic basis, three being termed "acute", five "subacute" and twenty-eight "chronic". Sixty-nine of the cases had ulcers in the duodenum, five being "acute", eight "subacute" and fifty-six "chronic". Five individuals each

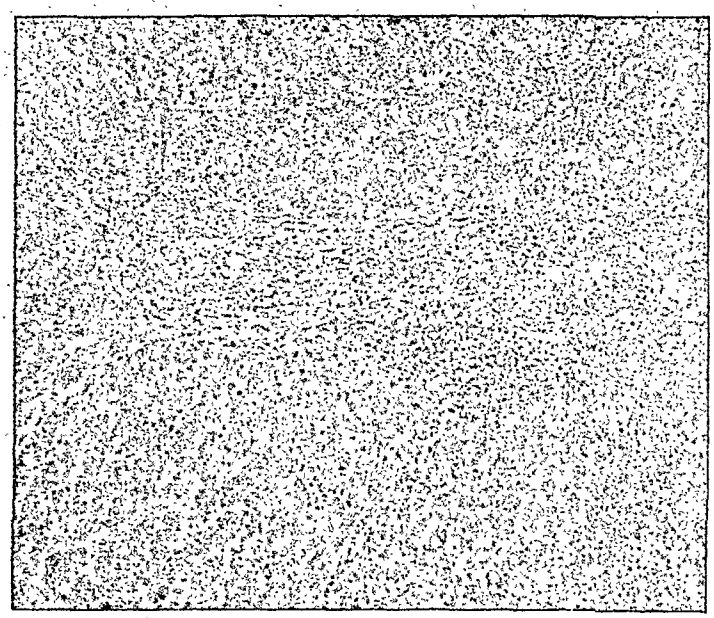


Fig. 1. This photomicrogram (x 100) shows the usual alterations in the portal areas of those livers included in Type I.

had both a gastric and a duodenal ulcer. It may be stated that the ratio of duodenal to gastric ulcer in this series was approximately two to one, whereas the usually accepted clinical figure is six to one.

Death resulted from the ulcer in thirty-two instances, twenty-one patients dying from perforation and peritonitis, nine from persistent hemorrhage, one from post-operative embolism and one from gastric obstruction. The remaining one hundred twenty-six patients died from various causes, as cardio-renal disease, pneumonia, malignancy, etc.; cirrhosis of the liver was responsible in only a moderate number of patients. It may be noted that clinical diagnoses of ulcer were made in only fifty-seven instances, the presence of the disease not being recognized in forty-three. In most of these unrecognized cases histopathologically, the ulcer was "healed" but apparently in several instances, even though the ulcers were not healed, the patients had had no symptoms.

For a control series, we selected one hundred consecutive patients in whom no ulcer was found at the *post mortem* examination. Two of these were diagnosed clinically as cirrhosis of the liver. There was one instance of acute yellow atrophy of the liver (from cinchophen poisoning) in this group. The selection of the control cases from consecutive autopsies was satisfactory because the average age of this group, 52.74, coincided very well with the average age of the ulcer group. As pointed out previously, the average age of the patients showing ulcer at autopsy was greater than was the average age of patients seen clinically with the disease. This was due to the fact that the majority (sixty-eight in our series) did not succumb to their ulcers but died of other diseases common to the fifth and sixth decades of life. The causes of death in the control series were essentially similar to those in the ulcer group with the exception of those patients who died from complications attributable to their ulcers.

The microscopic sections of the livers from the one hundred cases of ulcer and from the one hundred control cases were reviewed. In a few instances there were histologic changes in the liver which previously had not been recorded and which finally were considered as definite evidence of pathology. At the same time the microscopic sections of the pancreas from the patients with ulcer were studied. Except for the frequent occurrence of *post mortem* autolysis and the presence of malignancy in this organ in four instances, we were unable to detect any significant microscopic abnormality. For this reason that phase of the problem was disregarded and no study was made of the pancreatic sections from the control group.

MICROSCOPIC STUDY AND CLASSIFICATION OF THE LIVERS

The microscopic examination was made on blocks of liver which were removed *post mortem*. The blocks were fixed in Zenker's fluid and imbedded in paraffin. The sections were stained with eosin-methylene blue.

The *criteria which were used* in establishing four types of cases on the basis of the severity of the pathologic changes in the liver were not absolute. The variability of liver histopathology at different ages and in different diseases necessitated the use of a certain *flexibility of judgment in the categorical classification* of the many diverse pathologic changes which were encountered in this series. Despite the obvious difficulties of a satisfactory well-defined classification, certain facts were kept uppermost in mind and *four types were established,* as follows:

TYPE I—was characterized, as a rule, by a minimal degree of periportal fibrosis, a slightly increased number of infiltrating lymphoid cells in the periportal spaces and occasional proliferating bile ducts. The degree of periportal fibrosis was not uniform. Neither was it always apparent in all portal areas. In a few instances, there was a moderate engorgement of central veins and tributary sinusoids with a deposition of collagen in the central areas. The livers for the most part showed no gross evidence of cirrhosis. It must be stated that this group of cases was open to controversy because of the minor nature of the alterations and because of the frequency of similar histopathology in old individuals. Nevertheless, the degree of change was comparable with that which has been described repeatedly in association with chronic cholecystitis. Therefore, those who are familiar with the usual minor hepatic changes in instances of chronic cholecystitis can appreciate the extent of injury which in this series formed the basis of Type I. With some hesitation the described alterations in a few of the instances were attributed to chronic cardiac disease, although it must

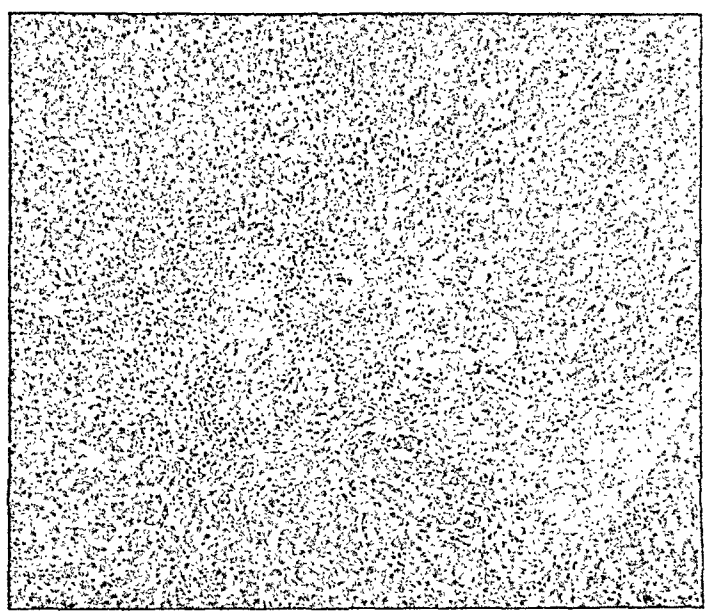


Fig. 2. This photomicrogram (x 100) shows a characteristic portal area of one of the livers classified as Type II.

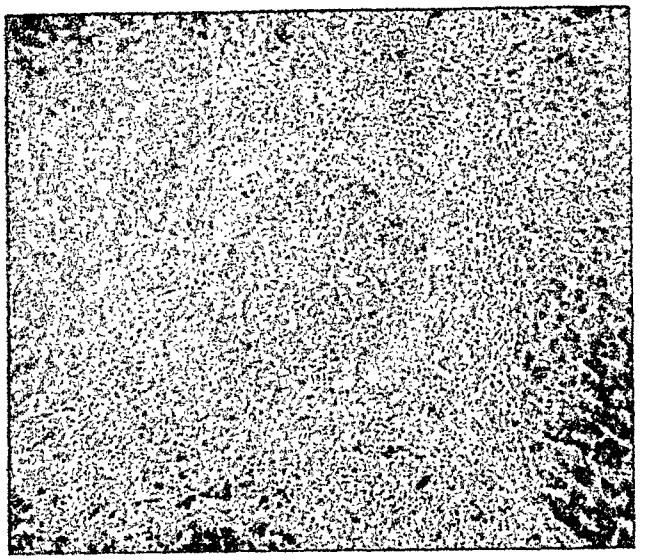


Fig. 3. This photomicrogram (x 100) exemplifies the type of pathology which usually was found in the livers which comprised Type III.

be recognized that factors other than cardiac decompensation may have played a *rôle*.

TYPE II—The livers which were regarded comprising this group generally were characterized by an easily detectable increase in the amount of periportal connective tissue and an increased number of infiltrating lymphoid cells, rare polymorphonuclear leucocytes and a few eosinophiles. There was evidence of proliferation of bile ducts in most of the portal areas. The parenchyma was involved only to a slight degree. In those cases revealing obstruction of the common bile duct, there were dilatation of biliary ducts and inspissation of bile in the canaliculi. Also, a few cases showed inflammation of the bile passages with numerous polymorphonuclear leucocytes in their *lumina* and in the regional connective tissue. A few of these livers exhibited gross evidence of cirrhosis. Several seemed to be instances of early portal cirrhosis. "Alcoholic hyalin" was demonstrable in three livers. Several were considered as examples of infectious biliary cirrhosis, either of idiopathic type or due to ascending cholangeitis which could be related, clinically, to pancreatitis, cholecystitis or to infection following obstruction of the common duct either by gall stones or carcinoma of the head of the pancreas. In these instances as well as those of Type I, care was taken to exclude the possible effects of an acute peritonitis secondary to perforation of peptic ulcer, inasmuch as peritonitis may cause an inflammatory reaction in the periportal areas with or without vascular thrombi. In this group, a number of cases, as well as a few with Type I changes, possibly were related to cardiac disease and its accompanying chronic passive congestion. The engorgement of central veins and tributary sinusoids with local degeneration of liver cells and not infrequent deposition of collagen in the central zones, prompted this assumption. One could not be certain as to how great an influence cardiac failure played in aiding the development of cirrhosis.

TYPE III—The livers which were so classified were examples of fairly well advanced cirrhosis. They were of the portal type. "Alcoholic hyalin" was found in four instances. Periportal fibrosis, numerous proliferating bile ducts, and a variable number of infiltrating lymphocytes, eosinophiles and polymorphonuclear leucocytes were the prominent findings. Numerous lobules of hepatic parenchyma, in all instances, parts had been destroyed by the pathologic process. One instance of obstructive cirrhosis with severe infectious biliary cirrhosis was assigned to this group. In another case, a history of chronic cardiac decompensation, evidence of chronic passive congestion and an irregularly distributed cirrhosis involving central areas, made it seem likely that cardiac failure to some extent may have influenced the cirrhotic process.

TYPE IV—The livers which comprised this group were instances of advanced cirrhosis. All were of the portal type. "Alcoholic hyalin" was demonstrable in one case. There were two instances of hemochromatosis. In each liver, many lobules had been destroyed and replaced by fibrous tissue. Broad bands of dense connective tissue infiltrated with numerous lymphocytes, eosinophiles and polymorphonuclear leucocytes and enclosing many proliferating bile ducts were prominent findings.

It seems unnecessary to dwell at great length upon the histologic findings in these four groups. The brief outlines which have been given cover the essential and characteristic features determining our classification. Unfortunately, there is no means by which one can convert the histologic findings into terms of function. Thus, in that respect their significance remains unknown. Any attempt to elaborate upon the vagaries of the relationship of histologic changes in the liver to disturbances in hepatic functional activity would be premature. Our purpose has been to describe as simply as possible the morphologic changes in the liver when it is associated with peptic ulcer.

ANALYSIS

In analyzing the material to determine the *relation of ulcer to liver disease*, it was found that fourteen of the seventy-two cases of cirrhosis of the liver (19.5 per cent) had associated typical ulcer of the stomach or the duodenum. These fourteen cases were included in the following analysis of the one hundred patients with ulcer.

From the other point of view, the *relation of liver disease to ulcer*, it was found that fifty of the one hun-

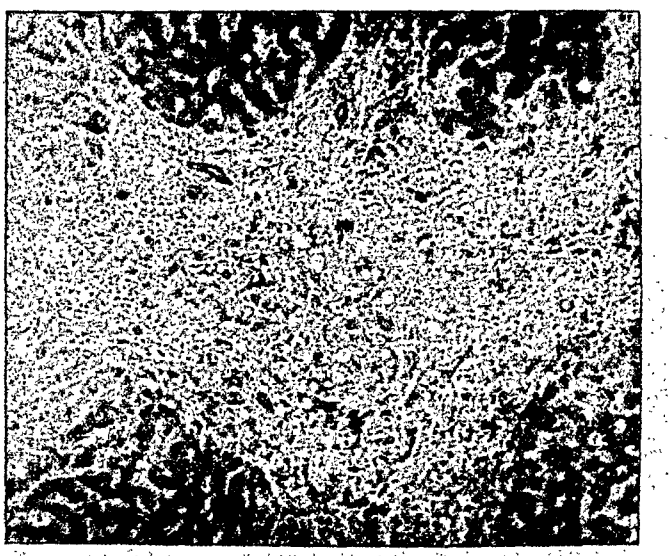


Fig. 4. This photomicrogram (x 100) exemplifies the severe hepatic cirrhosis which characterized all instances of Type IV.

dred ulcer cases showed definite histologic changes in the liver. Of these fifty with liver damage, seventeen had gastric ulcer, thirty-five duodenal ulcer and two each had both lesions. In the control series, thirty-six of the one hundred cases showed definite alterations in liver structure.

On further study, based on the type of changes in the liver as discussed under pathology, there were not only more patients with hepatic injury in the ulcer series than in the control group, but also the ulcer cases showed more definite lesions. Twenty-four of the ulcer cases showed Type I alteration. This was the largest single group. Eighteen of the cases showed Type II change, and six were of Type III. Of Type IV group, there were four cases with ulcer. (Table 1.)

TABLE I

Fifty Patients with Ulcer Showing Liver Change

Lesion	Type of Liver Change			
	I	II	III	IV
GASTRIC	10	5	1	1
DUODENAL	14*	13	5	3
TOTAL	24	18	6	4

*Two cases also had gastric ulcer.

A study of the *location of the lesion* or the frequency of duodenal as against gastric ulcer compared with the type of liver damage, did not add any information, so a further discussion from that standpoint has been omitted. By comparing the number of cases and the degree of liver change in the thirty-six of the control group, it was found that twenty-three showed Type I alteration. In eleven instances there were changes in the liver which placed them into Type II group, and there were only two cases showing Type III change. None showed a Type IV liver damage. (Table 2.)

TABLE II

Thirty-six Control Patients Showing Liver Changes

Type of Liver Change			
I	II	III	IV
23	11	2	0

A comparison of Tables 1 and 2 shows that the pathology in the liver was slightly greater in the ulcer group than it was in the control group.

In considering the *type* and the *degree* of liver change, it was apparent that many of the patients, in both the ulcer and the control groups, had other diseases which might be considered being responsible for the liver damage. These diseases include cholecystitis and cholangeitis, heart affections, syphilis, pancreatitis and primary and metastatic malignancy. There were twenty-six of the fifty cases with ulcer *and* liver changes in which the pathologic variations might be explained on the basis of these complicating diseases. Ten of these had cholecystitis and cholangeitis. As shown in Table 3, most of these cases had the minor Type I or II changes. There are only two cases showing Type III and none Type IV histopathology.

TABLE III

Twenty-six Patients with Ulcer in Whom the Liver Lesion Possibly Was Explained by Other Disease

Lesion	Type of Liver Change			
	I	II	III	IV
Cholecystitis, Cholang.	8	2	0	0
Heart Disease	5	4	1	0
Syphilis	2	0	0	0
Malignancy	0	3	1	0
TOTAL	15	9	2	0

A similar situation was found in the control group. Twenty-two of the thirty-six cases with hepatic changes essentially had like diseases as recorded in the ulcer group; possibly such accounted for the liver damage. Here, too, the great majority showed the minor degrees of injury to the liver. Fifteen had the changes of Type I, seven those of Type II, and none the changes of Type III and IV. (Table 4.)

TABLE IV

Twenty-two Control Patients in Whom the Liver Damage Possibly Was Explained by Other Disease

Lesion	Type of Liver Change			
	I	II	III	IV
Cholecystitis, Cholang.	10	3	0	0
Heart Disease	4	0	0	0
Malignancy	0	3	0	0
Pancreatitis	1	1	0	0
TOTAL	15	7	0	0

Thus, the liver changes in about half of the fifty cases wth ulcer and in about two-thirds of the thirty-six control cases might be attributed to some complicating disease.

Of the remaining cases, in both groups, in which evidence of hepatic injury was present, twenty-four with ulcer and fourteen of the control cases had no reasonable cause for the altered histology. These are shown in Table 5. There was no proof that the alterations were secondary to the ulcers. However, it must be admitted that an ulcer, particularly of the duodenum, might produce changes either by involvement of the common bile duct or by inciting an ascending lymphangeitis or cholangeitis.

Whether the liver injury was accounted for by other disease or not, only the cases with ulcer showed severe liver cirrhosis, ten of this group demonstrating Type III or IV change as against two of the control group who showed Type III alteration. Eight of these ten ulcer cases were in the group of twenty-four (Table 5) where no logical cause (excluding peptic ulcer) for the hepatic pathology was found.

To recapitulate, from a group of one hundred cases of typical peptic ulcer, fifty showed significant pathologic changes in the liver. In twenty-six of these fifty, the altered liver structure possibly was the result of

TABLE V

Twenty-four Ulcer and Fourteen Control Cases with "Idiopathic" Hepatic Injury

	Lesion	Type of Liver Change			
		I	II	III	IV
Ulcer Group	GASTRIC	4	2	0	1
	DUODENAL	5	5	4	3
	TOTAL	9	7	4	4
Controls	NO LIVER-DAMAGING DISEASE	8	4	2	0

other disease. In the remaining twenty-four the hepatic injury was "idiopathic". From a group of one hundred control cases, thirty-six showed change in the liver. In twenty-two of these thirty-six diseases of character similar to those complicating the ulcer group might account for the altered liver structure. In the other fourteen, the histologic change was unaccounted for. Assuming then, in both groups, that cholecystitis, heart disease, malignancy, etc., were the cause of the liver damage in the proportion stated, and omitting those cases, there were very few with "idiopathic" liver injury; twenty-four in the ulcer group and fourteen in the control series. The difference between these two groups seemed too slight to allow any definite conclusions to be drawn concerning the part played by changes in the liver as a basis for the etiology of peptic ulcer. The only feature noted was that there were more cases showing hepatic disease and more cases demonstrating Types III and IV injury in the ulcer group than there were in the control group. At present we are not prepared to evaluate the significance of these observations.

We consider the results of this study to be inconclusive. If the cause of ulcer is associated with a form of disturbance in the liver, the disturbance probably is functional in nature and is not associated with ordinarily demonstrable histologic changes. However, one can not disregard completely the relatively high incidence of ulcer (19.5 per cent) in the seventy-two instances of well-marked cirrhosis of the liver. This fact would seem to warrant appropriate studies for the exclusion of possible peptic ulcers as sources of gastro-intestinal hemorrhage in instances of cirrhosis of the liver.

SUMMARY AND CONCLUSIONS

There is considerable evidence to suggest that the biliary and pancreatic secretions play an important rôle in peptic ulcer. Heretofore, the neutralization of the acid gastric juice has been thought to be the chief function of these secretions, but the idea that when peptic ulcer arises there may be a "deficiency" of some substance in either one or both of these juices rather seems in keeping with the clinical picture of ulcer as it is understood today.

A review of the literature reveals that the most important surgical and chemical means used to produce chronic ulcers experimentally in animals, have been concerned with sidetracking or shutting-off these secretions, or with damaging the liver. A higher incidence of chronic ulcer was obtained by disturbing the liver or the bile flow than by interrupting the pancreatic secretion.

Since there were available no studies of the livers of patients with peptic ulcer in the literature, we have reviewed the microscopic sections of this organ in one hundred *post mortem* cases of peptic ulcer. For comparison, we have reviewed the microscopic sections of the liver of one hundred control patients coming to *post mortem* without an ulcer. A study of the pancreas from the ulcer cases returned no significant information so that phase of the investigation was discontinued.

1. From an arbitrary classification of liver damage, based on connective tissue overgrowth, cellular infiltration and degeneration of hepatic cells, it was found that there were more ulcer than there were control cases which exhibited liver damage.

2. The livers from the patients with ulcer showed more marked evidence of pathology than did those of the controls. This observation was in keeping with the high percentage (19.5) of peptic ulcers in seventy-two cases of advanced cirrhosis of the liver in the first group studied.

3. Essentially, like diseases in both groups, namely, cholecystitis and cholelithiasis, heart disease, malignancy, syphilis and pancreatitis, were possibly the agents producing the liver damage in many of the cases.

4. Omitting the cases with these complicating diseases, in twenty-four of the patients with ulcer and fourteen of the control patients, no reasonable explanation for the hepatic damage could be advanced.

5. If the cause of peptic ulcer is associated with a disturbance of the liver, the disturbance probably is functional in nature and not always is it associated with readily demonstrable histologic changes.

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THE EFFECTS OF DESICCATED HOG'S STOMACH IN ACHLORHYDRIA*

By

LEON SCHIFF, M.D.†

and

TOBA TAHL, A.B., M.D.†

CINCINNATI, OHIO

THE beneficial effects of preparations of liver or of hog's stomach (ventriculin) on the gastro-intestinal symptoms of pernicious anemia have been shown to be very striking. Long before there is an increase in the hemoglobin or red cells, marked improvement of the gastro-intestinal disturbance may occur. However, with the complete disappearance of dyspeptic symptoms there is no return of hydrochloric acid. This would indicate that the benefits obtained must be attributed to a substance contained in liver or the hog's stomach and that the substance is not free hydrochloric acid, as such is not a constituent of these preparations. Since the gastro-intestinal symptoms associated with other forms of achlorhydria may be similar to those seen in pernicious anemia and the pathological changes in the stomach identical (e. g., gastritis), it occurred to us to undertake the study of the effects of ventriculin in these achlorhydrias. After we had begun work on our problem, the use of hog's stomach in achlorhydria and in achylia gastrica was reported by Wilkinson and later by Eusterman. The former author obtained improvement of symptoms in cases associated with flatulent dyspepsia or diarrhoea. Eusterman mentioned the superiority of ventriculin, or its equivalent, to acid therapy. Levin has reported benefit from liver and liver extract in cases of achlorhydria.

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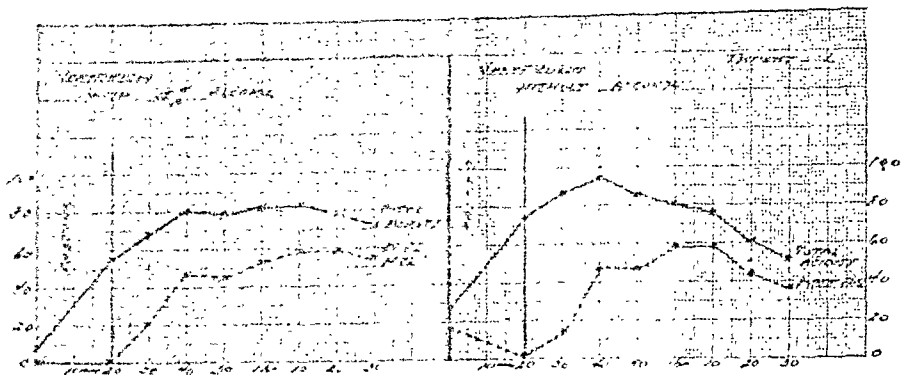
†From the Department of Internal Medicine, University of Cincinnati; Gastro-intestinal Clinic and Medical Service, Cincinnati General Hospital.

EFFECTS ON ACIDITY

Before clinical observations were begun, the effects of ventriculin upon gastric acidity were studied. As (desiccated) ventriculin tends to clump and stop up the Rehfuss-type tube, a specially prepared filtrate was used as a testmeal in the fractional analyses. This consisted of an aqueous extract of ventriculin made up in a concentration of 15 per cent alcohol; 1 c.c. being equivalent to 0.5 gm. of original material. In view of the fact that alcohol may stimulate the secretion of acid, control studies on gastric acidity were made with a purely aqueous filtrate and with a solution of 15 per cent alcohol. It is readily seen from the curves that the effects of the filtrate cannot be attributed to its alcoholic content (Figs. 1, 2).

Thirty cubic centimeters of filtrate were given after the removal of the fasting contents of the stomach and aspirations were made every ten to fifteen minutes until emptying had occurred. The curves were compared with those obtained with standard oatmeal gruel and following injection of histamine. The technique of Bloomfield and Polland was used in the tests performed with histamine, except that a constant dosage of 0.5 mg. of histamine was employed instead of 0.1 mg. per 10 kilos body weight.

Analyses were made in normals as well as upon patients with hypochlorhydria and achlorhydria (Figs. 3, 4, 5, 6).



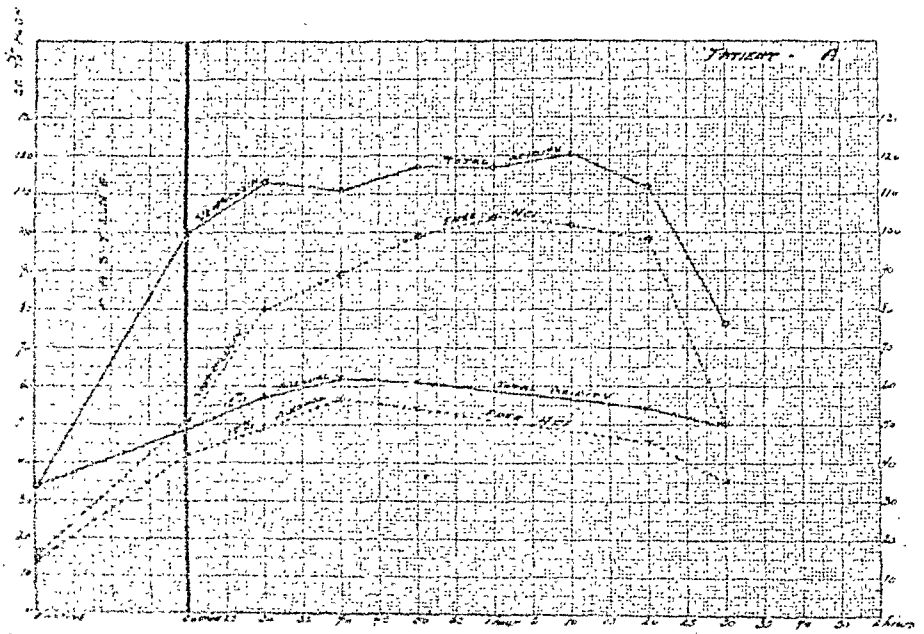
NORMAL

Fig. 1. Comparison of effects of a 15 per cent alcoholic Ventriculin filtrate with a non-alcoholic Ventriculin filtrate.

Study of the curves demonstrates that ventriculin produces an increase in the secretion of free hydrochloric acid. The degree of free acidity may be greater than occurs after injection of histamine, although in the majority of cases, it is less. The total acidity may be as high as, or higher than, that obtained with histamine. This may be due to the acidity of the filtrate itself. It is, of course, possible that the increase in the free acidity, at least in part, may be attributable to the protein content of ventriculin. It is interesting to note that a higher acidity may be obtained in normals as well as in cases of hypochlorhydria, when ventriculin filtrate (30 c.c.) is added to the oatmeal gruel, than when there are added 40 minims of dilute hydrochloric acid. Figure 6 shows the results in a case of hypochlorhydria.

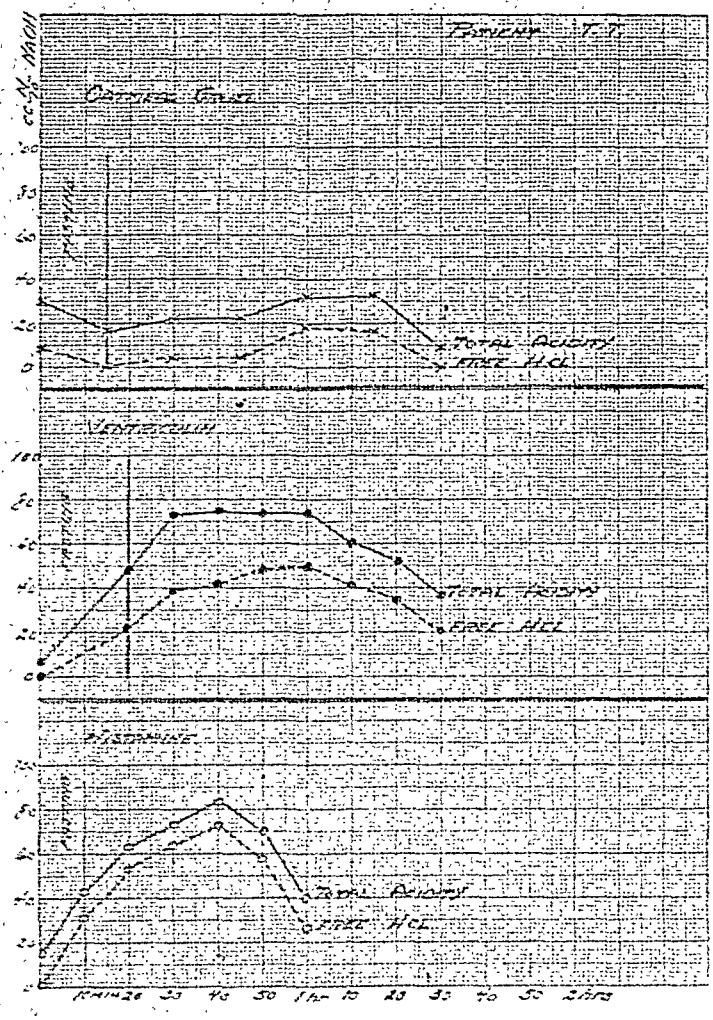
MOTILITY STUDIES

Studies of the effects of ventriculin upon the motility of the gastro-intestinal tract were undertaken in five patients who had achlorhydria and one who was normal. The patients were given 4 oz. of barium to which milk was added up to a total volume of 12 oz. The passage of the opaque material through the gastro-intestinal tract was observed fluoroscopically and drawings were made at each sitting. The studies were made at hourly intervals until the stomach was empty and also at nine, twenty-four and forty-eight hours after the ingestion of the meal. Control studies were made one week later with the use of a mixture containing 4 oz. of barium and 1 oz. of ventriculin filtrate in a total volume of 12 oz. of milk. The observations were checked at least once with both the ventriculin and control meals. No constant effect was noted upon the emptying time of the stomach or small intestine. In three individuals, there was distinct increase in the passage of the barium through the colon when the ventriculin was added. Unfortunately, an opportunity was not afforded for motility studies during attacks of gastrogenous diarrhoea, although one of the five patients studied gave a history of such attacks. In a normal individual, no effect was found upon the rate or character of the gastric or small intestinal motility but there was a definite increase in the rate of passage



NORMAL

Fig. 2. Comparison of effects of (aqueous) Ventriculin filtrate with alcohol (15 per cent).



NORMAL

Fig. 3. Comparison of effects of Ventriculin, Histamine and gruel.

of barium through the colon. The stimulation of colonic motility later was borne out by clinical observations which included several cases of uncomplicated chronic constipation.

CLINICAL OBSERVATIONS

The patients affected with achlorhydria were selected only after careful study. No instructions were given as to diet or hygienic measures. No attention was paid to the treatment of foci of infection and no medication was ordered except as included in the Case Abstracts. The patients generally were seen every two weeks and were subjected to a specially prepared *questionnaire* on each visit. The ventriculin generally was given in doses of 5 to 10 gms. exhibited in milk or in water fifteen minutes after meals. (Fruit juices, which afford a better vehicle, were omitted because of their acid content and the possibilities for misinterpretation of results).

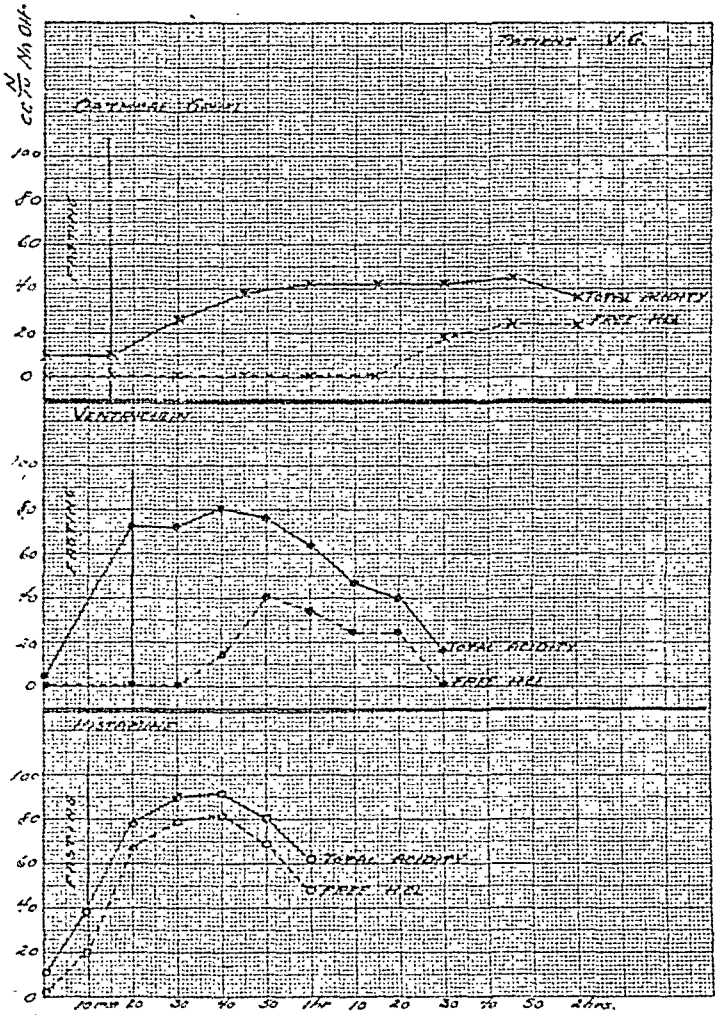
Ventriculin is a preparation of desiccated hog's stomach. It is acid in reaction but it does not give a test for free hydrochloric acid with Toepfer's reagent. It contains vitamin B and a varying quantity of pepsin (approximating 1 gr. per 3 gms. of material). The specially prepared ventriculin filtrate, of which 1 c.c. is equivalent to 0.5 gm. of ventriculin N. N. R., and a fat-free ventriculin (devoid of the anti-anemic principle) were substituted for the ventriculin in some of the patients with equally good effects. During control periods, either no medication was prescribed or hydrochloric acid was given in doses of 30 minims, administered in a glass of water which was taken fifteen to twenty minutes after meals.

The seven cases included in this report are part of a group of patients studied at the Cincinnati General Hospital within the past two years or more. Of the seven, three had achlorhydria and four achylia gastrica. The patients with achlorhydria presented, respectively, (1) gastrogenous diarrhoea, (2) chronic cholecystitis, and (3) ulcer-like syndrome without demonstrable ulcer. Of the four patients with achylia gastrica, three presented the same type of symptomatology as those with achlorhydria. The fourth had dyspeptic symptoms associated with constipation.

CASE REPORTS

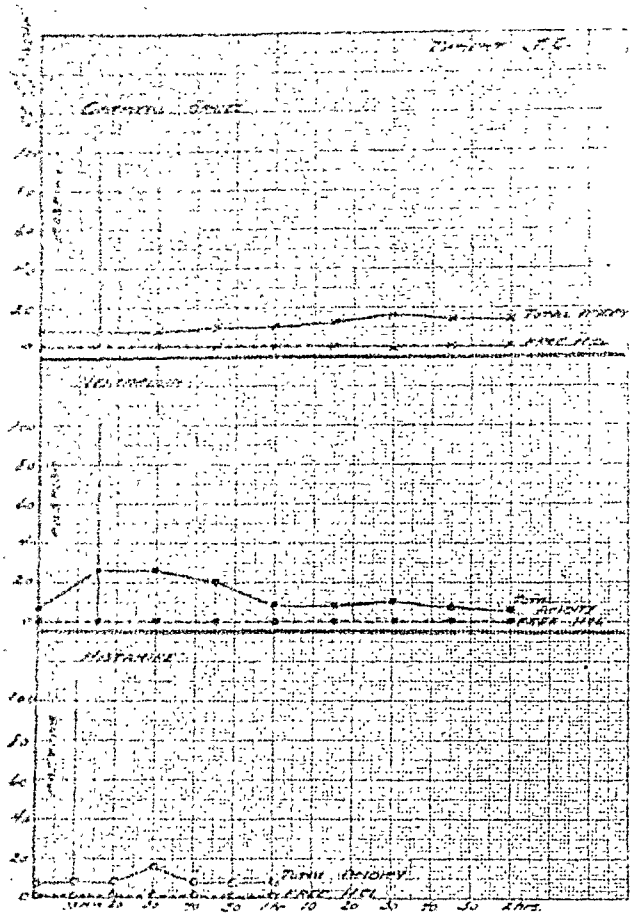
Case 1—M. M. (constitutional achylia; gastrogenous diarrhoea; hypochromic anemia). The patient, a student nurse, aged nineteen, first was seen January 19, 1932, complaining of marked fatigability of eight months' duration. She was so constantly tired that she spent every spare moment in bed. There was no glossitis, skin eruption or numbness or tingling of the extremities. For the month preceding our observation, she had been experiencing anorexia, nausea and vomiting, abdominal pain and attacks of diarrhoea which attacks occurred commonly in the morning. During these attacks the stools were watery and numbered six to eight daily. A maternal grandfather, uncle and aunt had died of pernicious anemia. The blood count exhibited 5,600 white cells, hgb. 62 per cent (Sahli), r.b.c. 3,600,000. Differential variation was: polys 58 per cent, lymphs 33 per cent, M. & T. 6 per cent, eosinophiles 3 per cent. The red blood cells and platelets appeared normal in form and size but showed moderate achromia. The patient's weight was 115 pounds.

The *physical examination* essentially was negative; she was normal vibratory sense. *X-ray examination* of the gastro-intestinal tract, including the gall bladder, was negative. *No free*



HYPOCHLORHYDRIA

Fig. 4. Comparison of effects of Ventriculin with Histamine and oatmeal gruel.



ACHLORHYDRIA

Fig. 5. Comparison of effects of Ventriculin with Histamine and oatmeal gruel.

hydrochloric acid was present upon fractional gastric analysis with an oatmeal gruel meal or after histamine.

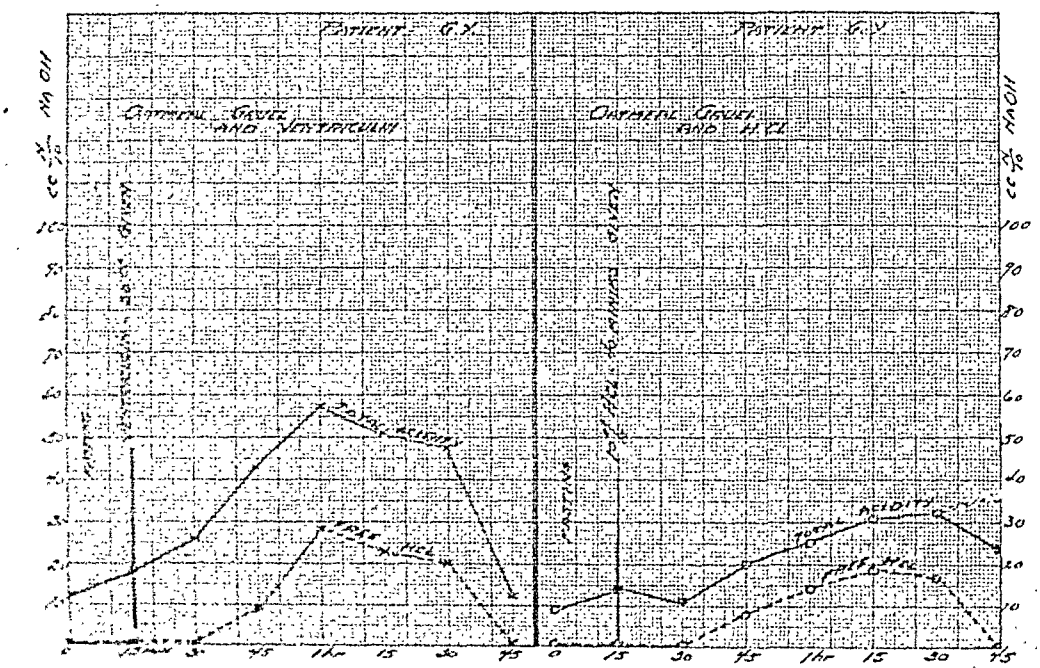
The patient was placed on 5 gms. of ventriculin after meals. Improvement in appetite occurred after one week accompanied by weight-gain of three pounds and disappearance of the clinical symptoms. Within one month, the hemoglobin rose to 74 per cent, and the red blood cells to 4.2 millions. Treatment was continued for a total period of three months, during which time the patient remained virtually symptom-free. The next three months gradually she reduced the ventriculin dosage to 10 gms. taken once weekly.

After this period the patient took ventriculin at rare intervals, notably when tired. When last seen (April 30, 1933), she stated that she had had two attacks of diarrhoea, each of which promptly had subsided upon the exhibition of a dose (10 gms.) of ventriculin. Her weight had increased to 130 pounds. Her red blood cell count was 4.2 millions; the hemoglobin 11.8 gms. per 100 c.c. (Iron purposely was omitted in treatment). The hematocrit reading was 38.23 c.c. per 100 c.c. and the M.C.V. 91 c.m.m.—findings in keeping with a secondary type of anemia. This patient still occasionally experiences fatigue but this is relieved promptly by ventriculin.

Case 2—H. B. (apparent achlorhydria; gastrogenous diarrhoea). The patient, a white male, aged sixty, entered the Medical Service of the Cincinnati General Hospital, December 20, 1931, complaining of intermittent diarrhoea of a year's duration. During an attack of diarrhoea the patient stated that he passed 10 to 20 or more watery stools a day. His appetite was poor. There was associated abdominal pain and flatulence. *Physical examination* was negative except for the presence of moderate generalized arteriosclerosis. There was no anemia. The urine was negative. *X-ray examination* of the gastro-intestinal tract, including the gall bladder, was normal. Microscopic *examinations of the stools* were negative, as also were tests for occult blood. *Proctoscopic examination* was negative. The patient was placed upon dilute hydrochloric acid for a period of three weeks which medication controlled the diarrhoea.

During the following year, the patient alternately was given dilute hydrochloric acid, ventriculin and ventriculin filtrate, to control attacks of diarrhoea, with equally good results. Accompanying the improvement in the diarrhoea there was a disappearance of abdominal pain and flatulence.

Case 3—J. McK. (achylia gastrica; chronic cholecystitis). The patient, a colored male laborer, aged forty-eight, was admitted to the Gastro-intestinal Clinic of the Cincinnati General Hospital on October 14, 1930, complaining of "stomach trouble" of a year's duration. He had been experiencing a



HYPOCHLORHYDRIA

Fig. 6. Comparison of effects of oatmeal gruel and Ventriculin with oatmeal gruel and acid.

cramp-like pain just above the umbilicus one and one-half to two hours after meals. There was occasional radiation of the pain to the substernal region. Frequent vomiting was experienced followed by relief of pain. Constipation was present. The patient had lost 12 pounds in the preceding six months. There were no attacks of abdominal colic. There was a history of anti-luetic treatment.

The *physical examination* disclosed no obvious anomalies. There was no anemia. *X-ray examination* of the gastro-intestinal tract was negative. The gall bladder failed to visualize on repeated X-ray examinations. Microscopic examination of "B" bile obtained by *transduodenal drainage* returned no cholesterin or calcium bilirubinate crystals. The *stools* were negative for occult blood. Blood Wassermann test and the urinalysis were negative.

This patient was given dilute hydrochloric acid for a period of rather longer than three months. There followed a decrease in the epigastric pain, nausea and vomiting and improvement in the general condition. Constipation was lessened. For the next two and one-half months, he was given from 10 to 30 gms. of ventriculin daily, with equally good results.

Then he left the city for about six months during which time he took no medication. There occurred a return of the epigastric pain, vomiting, constipation and anorexia. He then was given 5 gms. of ventriculin three times daily and prompt improvement followed. After two months, a fat-free ventriculin and ventriculin filtrate were tried and the results were equally good.

During a period of a year and a half, this subject underwent thirty fractional gastric analyses, fourteen of which followed the injection of histamine. At no time was either free hydrochloric acid or pepsin demonstrated as gastric analysis.

Case 4—C. E. (genuine achlorhydria; chronic cholecystitis). The patient, a white male, aged forty-eight, entered the Gastro-intestinal Clinic of the Cincinnati General Hospital, December 1, 1931, complaining of illness of two months' duration. He had experienced cramp-like pain beneath the right costal margin radiating to the epigastrium, belching, anorexia, flatulence and constipation. The pain commonly appeared about one-half to two hours after meals; it was relieved by soda. There was no history of attacks of abdominal colic. The general *physical examination* was essentially normal except for the presence of pyorrhea alveolaris. There was no anemia. Repeated *X-ray examinations* of the gastro-intestinal tract were negative. The gall bladder failed to visualize following the oral administration of *iodcikon*. The blood *Wassermann* reaction was negative. The *urine* was negative. "B" bile obtained on *transduodenal drainage* was negative microscopically. Tests for occult blood in the *stools* were negative.

The patient was given 5 gms. of ventriculin after meals for a period of three weeks. There was marked improvement in appetite and the disappearance of epigastric pain, constipation and flatulence. The patient then was placed on dilute hydrochloric acid for a period of three weeks with improvement but slightly less than that obtained with ventriculin. The acid medication was continued for a period of six more weeks, during which time there appeared a return of constipation. During the next month he was given one drachm of ventriculin filtrate after meals and constipation was relieved.

During the next five months, the patient was kept on ventriculin at his own request. Treatment then was discontinued. When last seen (April 3, 1933), he had gained thirty pounds in weight and, except for constipation, was free of symptoms. Two fractional gastric analyses with oatmeal gruel and three fractional analyses done after the injection of histamine proved the presence of pepsin but no free hydrochloric acid.

Case 5—G. H. (genuine achlorhydria). The patient, a white male, aged sixty, paperhanger, was admitted to the Gastro-intestinal Clinic of the Cincinnati General Hospital, May 23, 1932. He complained of having had a gnawing pain "in the stomach" for the past ten months. The pain occurred after meals; it was relieved by soda and food. There was nausea but no vomiting. The patient also recorded "debility" and loss of weight. The *physical examination* essentially was negative except for the presence of arteriosclerosis. Repeated *X-ray examinations* of the gastro-intestinal tract, including the gall bladder, were normal. The *stools* contained no occult blood.

On June 10, 1932, he was placed upon 5 gm. of ventriculin after meals and took this dose for a period of two and one-half months. There were marked diminution of the epigastric pain, disappearance of nausea and a weight-gain of five pounds. Then ventriculin was discontinued for a period of six weeks. Epigastric distress and nausea reappeared. Ventriculin therapy again was resumed for a period of two months and symptomatic improvement followed. Later he was given hydrochloric acid for several months; the results as satisfactory as those obtained from ventriculin.

Case 6—W. G. (achylia gastrica). The patient, a white laborer, aged forty-four, was admitted to the Gastro-intestinal Clinic of the Cincinnati General Hospital on December 2, 1930. He complained of having experienced a gnawing pain in his "stomach" for the past year and a half. The pain occurred one and one-half hours after meals and was relieved by ingestion of food. Vomiting occurred frequently.

Physical examination was negative, except for the presence of dental caries and pyorrhea alveolaris. There was no anemia. The blood *Wassermann* test was positive although the patient had received anti-luetic treatment. Two complete roentgen examinations of the gastro-intestinal tract, including the gall bladder, were negative. The stools exhibited nothing abnormal.

For three and one-half months, the patient was given 10 to 30 gms. of ventriculin daily. The epigastric pain disappeared and improvement occurred in his general condition. He gained three and one-half pounds. During the next ten months the patient did not return to the Clinic. He was seen at the end of this period and then complained of a return of epigastric pain, anorexia, vomiting and belching. One drachm of ventriculin filtrate after meals was then exhibited for six weeks. Marked improvement of symptoms followed accompanied by a weight gain of seven pounds. Then dilute hydrochloric acid was taken for four weeks. Improvement continued except for the appearance of constipation. During the period of observation, this patient was subjected to twenty-six fractional gastric analyses, eight of which were with histamine. Free HCl and pepsin never were demonstrated.

Case 7—J. C. (achlorhydria, genuine). The patient, a white male, aged sixty-two, machinist, was admitted to the Gastro-intestinal Clinic of the Cincinnati General Hospital, May 28, 1931, complaining of constipation of eight years' duration. In addition, he recorded anorexia, occasional nausea and vomiting and "cutting" pains in the abdomen. He had been taking cathartics regularly for eight years, with little benefit. The *physical examination* essentially was negative except for the presence of dental caries and pyorrhea alveolaris. There was no anemia. The blood *Wassermann* test was negative. *X-ray examination* of the gastro-intestinal tract, including the gall bladder, disclosed no abnormalities.

The patient was given mineral oil for two weeks without benefit except the relief of constipation. Then he was given 10 gms. of ventriculin, twice daily, for three weeks. There was improvement of appetite, diminution of abdominal pain and disappearance of constipation. A weight-gain of two and one-half pounds followed. The patient was given from 10 to 15 gms. of ventriculin daily for six months. During this time he remained symptom-free. Twenty-three fractional gastric analyses failed to reveal the presence of free hydrochloric acid. Over this six months' period he gained an additional five pounds. Ventriculin then was discontinued for seven weeks; there was a return of anorexia in spite of correction of constipation by laxatives. The patient was given hydrochloric acid for three weeks; constipation returned and with it, slight abdominal pain. The patient then was given ventriculin filtrate for two weeks and these symptoms disappeared. For four months he remained symptom-free on 15 gms. of ventriculin daily. During the next four months, the patient gradually reduced the dose of ventriculin to 10 gm. every other day and on this regime remained in comfort. When last seen (April 9, 1933), although no ventriculin had been taken for four months, he was still symptom-free with the help of an occasional laxative. A fractional gastric analysis at this date, following the injection of histamine, showed persistence of the achlorhydria. The patient requested that he be allowed to take ventriculin once weekly to relieve constipation.

In addition to the above described subjects, four patients with achlorhydria and gastro-intestinal symptoms were studied at the Branch Hospital in association with Drs. Christiansen and Lichleiter. All four were affected with far-advanced pulmonary tuberculosis. No evidence of tuberculous involvement of the gastro-intestinal tract could be detected after complete study. Two of the patients, twenty-six and thirty years old, respectively, exhibited achlorhydria and the other two, twelve and forty-seven years old, achylia gastrica. These patients were subjected to alternate two-month periods of treatment with ventriculin and to hydrochloric acid. The benefits obtained from ventriculin were much more striking than were those following the use of the acid. There was marked improvement in appetite in three of the four individuals. All experienced relief of abdominal pain. Nausea, present in three individuals (two with achylia), disappeared. Constipation, present in one with achlorhydria, was relieved. Diarrhoea, occurring in one with achlorhydria and in one with achylia, was definitely ameliorated. There was no anemia present.

In the patients with achlorhydria, a gain of five to seven and three-fourths pounds was recorded; one of the patients with achylia, gained ten pounds (Table 1).

TABLE I

Results in Four Cases of Tuberculosis (Ventriculin Therapy)

	Cases Present	Cases Improved
Abdominal pain	4	4
Epigastric pain	4	3
Anorexia	4	3
Flatulence	4	3
Constipation	1	1
Diarrhoea	2	2
Nausea	3	3

Three gained five to ten pounds (two-month period); one did not gain in weight.

CONCLUSIONS

1. The oral administration of single doses of ventriculin stimulates the secretion of free hydrochloric acid in normal individuals, patients with hypochlorhydria and apparent achlorhydria. The degree of acid secreted may exceed that produced after injection of histamine although, in the majority of patients, the converse is true with the dosages employed in this study. In genuine achlorhydria and achylia gastrica, no secretion of free hydrochloric acid results following ventriculin therapy.

2. The prolonged administration of ventriculin to patients with genuine achlorhydria or achylia gastrica may cause disappearance of symptoms without the return of free hydrochloric acid. (In three patients, twenty-four, twenty-six and thirty fractional gastric analyses done respectively during a period of over a year, failed to demonstrate a return of free acid.)

3. Benefit consists chiefly of improvement of appetite, lessening of abdominal pain and discomfort, lessening of nausea, gain in weight, disappearance of constipation or of diarrhoea. Equally good results have been obtained with fat-free ventriculin (devoid of anti-anemic factor) in some patients.

4. The administration of ventriculin is equally beneficial in cases of achlorhydria and achylia gastrica. This suggests that a common factor is lacking in both these conditions which factor probably is present in the desiccated hog's stomach. Evidently, this is not the anti-anemic factor.

5. The benefits obtained from ventriculin generally depend upon its continuous administration. Withdrawal may result in a return of symptoms. In some instances, small doses, taken at intervals, may be adequate to keep the patient symptom-free.

6. The administration of ventriculin may prove very helpful in instances of achlorhydria associated with pulmonary tuberculosis.

7. The value of ventriculin as a measure prophylactic against the development of pernicious anemia would appear to be self-evident.

8. The results obtained during our study would seem to indicate that the symptomatology associated with achlorhydria is due not to the achlorhydria *per se* but to the lack of an unknown substance present in desiccated hog's stomach. Probably this substance is a physiological constituent of the normal gastric secretion.

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THE SPECIFICITY OF THE COMPLEMENT FIXATION TEST FOR AMEBIASIS*

By

EMIL WEISS, M.D.*

and

LLOYD ARNOLD, M.D.*

CHICAGO, ILLINOIS

A METHOD of increasing the sensitiveness of a complement fixation procedure for detecting antibodies against *Endameba histolytica* in the serum has been recently described (Weiss and Arnold (1)). Various complement fixation technics previously have been described by several workers. The practical value of any serological method rests as a rule on the degree of its specificity. This depends largely on the sensitiveness of the principle reagents used, namely, the serum and the antigen. Craig (2) and (3) was the first one to observe that a certain number of Wassermann positive sera gave also positive tests for amebiasis by his method. Craig at first assumed that the Wassermann was specific and his complement fixation test was nonspecific in certain rare cases; however, there was some evidence of gastro-intestinal disorders in these patients. In a later report (4) Craig finds that in properly treated amebic cases, which were positive with Wassermann and Kahn tests for syphilis and complement fixation test for amebiasis, the latter becomes negative after specific treatment for amebiasis while the other two remain positive. Syphilitic infection does not give positive reaction with the complement fixation test for amebiasis unless there is a simultaneous infection with *Endameba histolytica*.

*From the Department of Bacteriology and Preventive Medicine, University of Illinois, College of Medicine, and Research Laboratories of the Illinois Department of Public Health, Chicago.
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In order to explain these positive reactions several possibilities had to be considered: (1) these patients may have both infections—syphilitic and amebic; (2) these patients may have syphilis, simultaneously giving a nonspecific ameba complement-fixation test; (3) the patients may have an amebic infection giving a nonspecific Wassermann reaction; (4) the patients may have neither syphilitic nor amebic infection but some other protozoal or bacterial infection.

In order to improve the procedure for the complement-fixation test for amebiasis as well as the sensitivity, extensive studies of the ingredients used in the test had to be made. Special consideration is required for the study of antigens and serum. This became imperative due to the difficulties of some workers in preparing sufficiently strong antigens for the test. In our work we found that the sera of many amebiasis patients possess relatively small amounts of antibodies. This was overcome in our own procedure by using larger amounts of patient's serum. It remains, therefore, to determine to what extent the observations and principles used in other complement-fixation tests apply to the antigens used in the complement-fixation test for amebiasis.

I. *Preparation of the Antigen.* The 48-hour growth from ten culture tubes of *Endameba histolytica* is transferred to centrifuge tubes and centrifuged. The supernatant fluid then is removed, the sediment resuspended in normal saline and again centrifuged until the supernatant fluid appears quite clear. The sediments of the centrifuge tubes then are dried, the residue is scraped off with a knife and placed in a wide tube or flask and covered with 50 c.c. of absolute alcohol. The extraction is carried on for 48 hours at 55 degrees C. in a water bath. The extract is concentrated by evaporation of the alcohol, until it assumes a distinctly yellow color. The extract is then filtered and preserved in tightly stoppered bottles. Rubber stoppers are preferred. The extract is now ready for titration. The details of the procedure are given in the original article (Weiss and Arnold (1)).

II. *Titration of the Antigen.* Twenty Wassermann tubes are placed in two rows in a rack. Increasing amounts of the extract, 0.05, 0.1, 0.2, 0.4, 0.6, 0.8 c.c. diluted 1:10 and 0.5, 0.6, 0.7, 0.8 c.c. diluted 1:5 are placed in the ten tubes of the front row, and the same amounts in the corresponding ten tubes of the back row. Normal saline is added to each tube to make up 0.8 c.c. Each tube of the front row received 1 c.c. of an inactivated negative serum and each tube of the back row received 1 c.c. of a strong positive (amebic) serum. Each tube of both rows received 0.1 c.c. of a 50 per cent complement dilution. The tubes are shaken vigorously and placed in a water bath for 30 minutes at 37 degrees C. After the incubation, five units of amboceptor in 0.5 c.c. saline and 0.1 c.c. of a 25 per cent suspension of washed sheep blood cells are added to each tube. The tubes are again shaken vigorously and returned to the water bath for 30 minutes at 37 degrees C. The results are then read. The largest and smallest amount of the antigen giving complete inhibition with a positive serum and hemolysis with a normal serum is determined. The amount of antigen midway between the largest and smallest specific dose is then selected as the antigenic dose. The details are given in the original article (1).

III. *The Zonal Reactions of the Amebic Antigens.* Each batch of the prepared antigens was titrated so as to determine its zonal reactions. The following zones were observed from smaller amounts upward toward larger doses: (a) The inefficient zone, the normal and the amebic serum giving complete hemolysis; (b) the lower margin of the specific zone, the amebic serum giving only incomplete hemolysis; (c) the upper margin of the specific zone with amebic sera showing complete inhibition of hemolysis, and the normal sera giving complete hemolysis. The wider this zone is the more satisfactory is the antigen; (d) the lower margin of the inhibition zone, the amebic sera showing complete inhibition of hemolysis, the normal sera showing more or less inhibition; (e) upper margin of the inhibition zone, the normal and amebic sera showing alike complete inhibition of hemolysis; (f) hemolytic zone, the normal and amebic sera showing alike hemolysis; (g) the precipitation zone, the normal and amebic serum showing precipitation of proteins, namely, the red blood cells. In all tested antigens it was found that the lower and upper margin of the inhibition zone always precede the hemolytic zone. On the other hand the specific zone is preceded by the lower specific sub-zone and followed upward by the lower inhibition sub-zone. These constant and uniform findings justify the elimination of a special titration for inhibitive and hemolytic properties of the antigens. The titration of the antigens in our procedure includes the entire complete specific zone and adjoining portions of the lower specific sub-zone and the lower inhibition sub-zone. Amebic antigens resemble the Wassermann antigens with regard to zonal reactions (Weiss (5)). To what extent the ameba lipoids resemble the lipoids from Wassermann antigens with regard to zonal reactions remains to be determined.

IV. *Factors Having Influence on the Preparation of Antigens.* In the study of optimal conditions for the preparation of amebic extracts, it appeared advisable to consider various factors which may have a direct bearing on the results. The use of amebae washed from the culture medium without drying resulted in extracts which were always weak in antigenic quality. This could be anticipated, due to the dilution of the solvent by the watery suspension of the amebae. On the other hand, washed ameba cultures which were dried and pulverized proved to be satisfactory material for extraction with alcohol. Again, in the process of extraction of dried and pulverized amebae, the temperature and duration of extraction appeared as additionally important factors having an influence on the strength and sensitiveness of the antigens. In order to determine the importance of temperature extraction on the antigenic quality of the extracts, extractions were carried out at ice box and room temperatures, at 37 degrees C. and 55 degrees C.; the latter two extractions were performed in the water bath. The duration of extraction was in most instances one week. The initial ratios between solvent and the material to be extracted were: 50 c.c. absolute alcohol to the powder of ten dried washings of ameba cultures. The findings of these experiments indicate that extracts at room and ice box temperatures, when concentrated by evaporation, are unsatisfactory for complement fixation. The extracts prepared at 37 degrees C. are usually weak, and their sensitiveness is slightly increased by evaporation. The extracts prepared at 55 degrees C. are useful within forty-eight hours after extraction has been concluded. The experiments carried out to determine the influence of the length of extraction can be summarized as follows: Regardless of the duration of extraction, antigens prepared at ice box and room temperatures appear worthless. Antigens prepared at 37 degrees C. are too weak to be useful after two weeks of extraction, the sensitiveness being somewhat increased by subsequent concentration by evaporation at 37 degrees C. The extracts prepared at 55 degrees C. appear useful within two days; their strength increases greatly within one week, slightly more within the second week, but longer extraction does not increase antigenic content. While the ratios between solvents and tissues to be extracted were of great importance in antigens used in Wassermann and precipitation tests, the ratio as an essential factor was greatly reduced in importance in preparation of amebic antigens. The extract when finished can be concentrated until it attains a sufficient degree of sensitiveness. Therefore the initial ratio between solvent and amebic powder is of secondary importance.

V. *Fractional Extractions.* Pulverized beef heart is usually used for extraction of lipoids in preparation of Wassermann and precipitation antigens. The alcohol soluble lipoids of the beef heart are almost insoluble in acetone, ether, chloroform, benzol and xylol, only a small fraction being soluble. Lipoids soluble in acetone, ether, chloroform, benzol and xylol are almost insoluble in alcohol, only a very small fraction being soluble. The acetone soluble lipoids are less useful for the Wassermann test than the alcohol soluble ones and are useless for the Kahn test.

The lipoids extracted with alcohol from pulverized amebae show different properties than those of the beef heart. In order to determine the fractional properties of amebic lipoids from 50 c.c. of a satisfactory alcoholic extract, the alcohol was removed by evaporation and an attempt was made to redissolve the residue in 50 c.c. acetone. The residue did not redissolve. The acetone was then removed by evaporation and a similar attempt made with ether. The residue did not redissolve. The residue, on the other hand, dissolved completely in chloroform, benzol and xylol. In a similar manner 50 c.c. of a satisfactory acetone extract were evaporated at 37 degrees C. and the residue could be completely redissolved in alcohol.

The application of Kolmer's method of preparation of antigens to amebic extracts does not appear justified inasmuch as alcohol and acetone give almost equally useful soluble antigens. The discard of the acetone soluble substances from amebae represents therefore a direct waste of useful antigen.

VI. *Acetone.* Seven different extracts were prepared with acetone in an identical manner as previously described for the alcoholic extracts. All the prepared acetone extracts were found useful for the test. In three instances, the upper specific sub-zone was narrower than observed in alcoholic extracts. Otherwise, the zonal reactions were very similar to those of alcoholic extracts. Based on these findings the acetone antigens may be considered as only slightly inferior to alcoholic extracts.

VII. *Cholesterol and Lecithin.* It appeared to us worthwhile to determine to what extent these substances are suitable to increase the sensitiveness of amebic antigens. Cholesterol was added to the alcoholic extracts up to the concentration of 0.3 per cent and lecithin up to 0.4 per cent. The results obtained are quite contrary to those observed in the use of Wassermann and Kahn antigens. It is an established fact that the cholesterol increased the sensitiveness of almost every Wassermann antigen, and in the Kahn test and other syphilitic precipitation tests the cholesterol is an essential constituent without which the antigen is useless. It was found that the addition of cholesterol or lecithin to amebic antigens renders them non-specific. All syphilitic sera tested (386) gave positive reactions and negative results using the same extract without cholesterol or lecithin. The uselessness of cholesterol and lecithin as "sensitizers" for amebic antigen appears thus established. These results eliminate also the possibility of developing a precipitation test for amebiasis similar to that of Kahn or other precipitation tests for syphilis.

VIII. *Specificity of Amebic Complement Fixation Test in Regard to Syphilis.* Craig (4) found the Wassermann and Kahn test positive in a small percentage of amebic sera which he examined. In our own work a similar observation has been made. Of 947 sera negative for amebiasis, eighteen or less than 2 per cent were Wassermann or Kahn test positive. Among one hundred ninety-two positive amebic sera examined, we found fourteen or less than 8 per cent gave positive Wassermann or Kahn reactions, (Table I). Among those fourteen cases positive both

TABLE I

Specificity of Ameba Antigens with Regard to Syphilis

	Craig complement fixation test for Amebiasis		Weiss-Arnold complement fixation test for Amebiasis	
	Positive	Negative	Positive	Negative
Number of sera examined	110	676	192	947
Positive Wassermann and Kahn tests	15 or 13.6%	56 or 8.2%	14 or 7.2%	18 or 1.9%

for amebiasis and syphilis, only eleven offered sufficient clinical data for the interpretation of the results. These eleven patients had never had symptoms or received treatment for syphilis, while ten had at different times had gastro-intestinal disturbances which in eight cases were diagnosed as ulcerative or mucous colitis. No satisfactory laboratory examinations were made at the time of the intestinal disturbances. Only one among the eleven cases did not reveal any history or symptoms pointing toward amebic dysentery. At the time the Wassermann and amebic complement fixation tests were performed, the syphilitic tests were ordered as a matter of routine and not because of suspicious symptoms indicating syphilis.

IX. *Specificity of Amebic Antigens with Regard to Other Protozoal Diseases.* Cross-complement fixation tests were performed with a series of amebic antigens and immune serum of sheep prepared with trypanosoma equiperdum. Similarly complement fixation tests were performed with extracts prepared from trypanosoma equiperdum and immune sera prepared against ameba extracts. In addition, complement fixation tests were performed between amebic antigens and sera of rabbits inoculated with treponema pallidum. These rabbit sera gave positive Wassermann and Kahn tests. Conversely the alcoholic extracts of treponema pallidum were tried against amebic immune sera. Noguchi (6) was the first to introduce aqueous suspensions of cultures of spirocheta pallidum as antigens in the Wassermann test. The unsatisfactory results he obtained could be anticipated on account of the crude preparation of these antigens. Far better results were obtained by Craig and Nichols (7) by adding to the liquid part of Noguchi's medium ten times its weight absolute alcohol for ten days. The filtered extract was then evaporated to one-third its volume and titrated in dilution 1:10.

For our cultivation of treponema pallidum a serum broth (1:4) containing an 0.1 neutralized cysteine hydrochloride was used. Four-week-old cultures were evaporated and the extracts prepared in the same manner as described for Endameba histolytica. All these cross-complement fixation tests as stated gave negative results.

X. *Specificity of Amebic Antigens with Regard to Bacterial Infections.* Complement fixation tests were performed with sera: six patients with pneumonia, four with typhoid fever, two with scarlet fever, one with measles, two with diphtheria and one with tularemia. The results were in all instances negative. In an identical manner, complement fixation tests were performed with immune sera prepared by immunizing rabbits with the following bacteria: typhoid, paratyphoid A and B. Salmonella psittacosis, proteus, B. dysenteriae Flexner and Shiga. The results were entirely negative. Immune sera of rabbits prepared with Monilia Albicans strains gave also negative complement fixation tests.

XI. *Amebic Antigens as Antibody-Formers.* In order to secure a steady supply of positive amebic sera, six rabbits were immunized with washed cultures of *Endameba histolytica* and six rabbits were immunized with a saline dilution of an alcoholic Endameba extract. Increasing amounts of the described antigens were inoculated intravenously at two-day intervals. The total number of inoculations were six. One or two weeks after the last inoculation the sera of the rabbits were tested for the presence of complement fixing bodies. It was found that all the above sera gave positive complement fixation, some (8) of them even in the dilution 1:100. The sera of two other rabbits immunized with residues of dried ameba cultures after extraction with alcohol also gave positive complement fixation tests. The least toxic reactions to inoculations were those with saline dilutions of alcoholic antigens, more toxic were those with fresh ameba cultures, while the most toxic appeared to be the residues of ameba cultures after extraction with alcohol. The alcohol extracts proved to be, as judged by the results of complement-fixation, equally useful as the whole ameba cultures for the formation of complement fixing bodies, (Table II).

XII. *Amebic Sera in Relation to Wassermann Reaction and Kahn Test.* Amebic immune rabbit sera prepared either with washed amebae cultures, diluted extracts or residues after preceding alcohol extraction, gave in all instances positive Wasser-

TABLE II

Specificity of Amebic Antigens with Regard to Other Protozoal Diseases

Antigens (1:10)	Complement Fixation Test with Immune Sera Against:					
	Trypanosoma equiperdum	Endameba histolytica			Treponema pallidum	
		39	42	45	21	22
Alcoholic amebic extract 1	–	++++	++++	++++	–	–
Alcoholic amebic extract 2	–	+++	++++	++++	–	–
Alcoholic amebic extract 8	–	++++	++++	++++	–	–
Alcoholic amebic extract 18	–	++++	++++	++++	–	–
Alcoholic extract trypanosoma equiperdum	++++	–	–	–	–	–
Alcoholic extract treponema pallidum	–	–	–	–	++++	++++
Alcoholic extract endameba coli	–	–	–	–	–	–

TABLE III

Wassermann and Kahn Tests with Amebic Immune Sera

Antigens (1:10)		Immune Sera Against: Washed Ameba Cultures			Diluted Alcoholic Amebic Extracts			Ameba Residue after preceding alcohol extraction	
		20	31	43	39	42	45	10	
Wassermann Test with:	Plain alcoholic beef-heart extract	+++	++++	++++	+++	++++	++	+++	+++
	Cholesterolized beef-heart extract	++++	++++	++++	++++	++++	+++	+++	++++
	Kolmer's Antigen	++++	++++	++++	+++	++++	+++	+++	+++
	Kahn's Antigen	++++	++++	++++	++++	++++	++++	++	++++
Kahn Test		+++	++++	++++	+++	+++	++	+	+++

mann reaction and Kahn test. Similar were the results with a limited number of strong positive amebic sera from patients with a definitely established clinical and laboratory diagnosis of amebic dysentery without any evidence of syphilis, (Table III).

XIII. *Beef-heart Lipoid Immune Serum in Relation to Amebic and Bacterial Extracts.* Complement fixation tests were performed using inactivated sera from six rabbits immunized with beef-heart lipoids and a series of alcoholic and acetone ameba extracts. Although all controls gave the proper reactions, the lipoid beef-heart antisera gave in all instances strong positive reactions. Beef-heart lipoid antigen gave also strong positive fixation with its corresponding immune serum. Complement fixation between a series of bacterial alcoholic extracts and the beef-heart lipoid immune serum were negative. Those results indicate that beef-heart lipoids can produce complement fixing bodies which give positive results not only with their own antigen but also with lipoids of protozoa but not with lipoids obtained from bacteria and yeasts. The beef-heart lipoid antiserum appears as much non-specific as its antigen, (Table IV).

TABLE IV

Beef-heart Lipoid Immune Serum in Relation to Amebic and Bacterial Extracts

Antigens (1:10)	Complement Fixation Test With: Immune Serum Against Beef-heart Lipoids: 1	2	3	4	5	6
Alcoholic ameba extract No. 16	++++	++++	+++	++	++++	++
Alcoholic ameba extract No. 17	++++	+++	+++	+++	++++	++
Alcoholic ameba extract No. 25	++++	++++	+++	+++	++++	+++
Acetone ameba extract No. 46	++++	++++	++++	+++	++++	++++
Alcoholic extract Beef-heart	++++	++++	++++	++++	++++	++++
Alcoholic extract B.typhosus	–	–	–	–	–	–
Alcoholic extract B paratyphosus A	–	–	–	–	–	–
Alcoholic extract B.paratyphosus B	–	–	–	–	–	–
Alcoholic extract B.dysentariae Flexner	–	–	–	–	–	–
Alcoholic extract B dysentariae Shiga	–	–	–	–	–	–
Alcoholic extract Monilia albicans	–	–	–	–	–	–
Alcoholic extract Aspergillus niger	–	–	–	–	–	–

DISCUSSION

The analytical study of amebic antigens and the factors which influence the quality of the extracts has shown that useful antigens can be easily obtained if the simple procedure outlined here is followed. The findings indicate that extraction at 55 degrees C. for two weeks is the procedure if a thorough extraction of useful antigen is desired. Alcohol or acetone extracts are of such strength that the recommended additional concentration by evaporation is usually unnecessary. These extracts are highly specific. The fact that they give positive complement fixation with beef heart lipoids immune sera does not affect their specific character. According to Sachs (8) the sensitiveness of specific antigens increases with the addition of cholesterol without the loss of their specific character. The addition of cholesterol or lecithin to amebic antigens resulted in their complete loss of specificity giving positive complement fixation with syphilitic serum and immune sera of other protozoa. Sachs' observations do not seem to apply to the amebic antigens. As a matter of fact, the beef heart lipoid antisera give complement fixation with any extracts containing animal lipoids. The lower percentage of positiveness in the amebic complement-fixation test as compared with the Wassermann and Kahn test, is caused by small amounts of antibodies and not due to the weakness of antigens. This has been shown with amebic immune serum, which gave consistently strong positive complement fixations, even in high dilutions. If the antigens were weak they could not give strong reactions regardless of the titer of the immune sera. The positiveness of the test was increased by using 1 c.c. of patient's serum instead of 0.1 c.c., thus increasing the amount of antibodies eventually present in the serum. If the antigens were only moderately useful, the increased amount of serum used in the test would not appreciably alter the results. The Wassermann and Kahn tests, performed with immune sera of *E. histolytica, treponema pallidum* and *trypanosoma equiperdum* gave positive reactions; positive reactions were also obtained with some amebic patients without any symptoms or history of syphilis. Assuming that these nonspecific reactions were caused by the nonspecific antigen used in the Wassermann and Kahn test, a specific antigen was prepared from *treponema pallidum* in a similar way as that for amebae. Wassermann tests performed with this extract gave positive reactions with the sera of rabbits infected with *treponema pallidum*, with syphilitic sera, but negative results with sera of rabbits immunized with ameba or with the immune serum against *trypanosoma equiperdum*. These findings would indicate—and we would recommend—the use of a spirochete antigen for those few cases where the complement-fixation test for amebiasis is positive and the usual Wassermann and Kahn tests are also positive.

The alcoholic extracts of *E. histolytica* give specific complement fixation and can also be used to produce specific immune serum; they are less toxic than the washings of ameba cultures when inoculated in animals. Whether these extracts can be used to produce active or passive immunity remains to be determined by additional studies.

SUMMARY

1. Alcohol and acetone extracts of *E. histolytica* yield a specific antigen. Specific antiamebic serum can be produced by the injection of this antigen.

2. The beef-heart lipoidal antigens used in the Wassermann and Kahn tests can give nonspecific reactions not only with serum of amebic dysentery patients, but also with immune serum produced from various protozoa. These beef-heart lipoids can produce antisera which can be shown to contain nonspecific antibodies.

3. When complement-fixation tests are positive for both amebiasis and syphilis (Wassermann) the Wassermann reaction can be checked by using a specific spirochete antigen instead of the beef-heart lipoids.

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ABSTRACTS

GILSHANNON, B. J.

Case of Terminal Ileitis of Unknown Origin.

An American woman, aged 26 years, a housewife, enjoyed good health until recently. So far as she knows, there was no exposure to tuberculosis. She had a mild influenza five years ago. There have been no other respiratory infections. Digestion was always good, and the bowels moved well. Her weight has remained steady at about 110 pounds. There has been no trouble with menstruation or urination.

The patient came complaining of intermittent, cramp-like pain in the epigastrium which had been present for four days. She had been nauseated and vomiting for twenty-four hours. There was a similar attack a month previously. Just before the present attack, she had a severe cold, and felt bad for a week afterwards. She felt very tired. At first the epigastric pain was worse after a heavy meal; later, it came at any time, either when eating or an hour or two later. Drinking cold water once produced severe pain. The jar produced by stepping off a curb made the pain more severe. The bowels moved every day but she took several cathartics which caused the pain to be much worse.

Examination showed a woman who apparently was suffering severe pain in the lower abdomen. Temperature and pulse were normal. The abdomen was extremely tender, especially in the right lower quadrant, but there was no rigidity and no distension. No mass could be felt on examination through the vagina and rectum. The rest of the physical examination showed nothing wrong. The hemoglobin was a little low. The urine was normal. The leucocyte count was 9,000. The Wassermann reaction was negative. A "flat" film showed one or two loops of bowel filled with gas and with a suggestion of the markings which are indicative of obstruction. A diagnosis was made of partial obstruction of the ileum, and the patient was operated on.

At operation, the entire cecum and about half of the ascending colon, together with the last six inches of the terminal ileum, were found to be thickened and reddened. All of the mesenteric nodes draining this region were enlarged; some were the size of walnuts. The appendix was also thickened. Some of the nodes were removed and the pathologist reported an inflammatory reaction. There was no suggestion of cancer, tuberculosis or Hodgkin's disease.

The abdomen was closed and the patient appears now to be recovering under a hygienic regimen with periods of rest and heliotherapy. She is gaining in weight and there have been no further symptoms.

H. J. Wolff (Rochester, Minn.).

GRAY, IRVING.

External Trauma in Relation to Ulcer of the Stomach and Duodenum. Am. Int. Med., VII, 1493, (May) 1934.

The author briefly reviews the American literature on the relationship of trauma to peptic ulcer and comments on the relative infrequency of reported cases as compared with the more apparent readiness with which Continental physicians accept traumatic ulcer as a clinical entity. The author adds five cases to the literature in which trauma was considered to be a factor, either in the production of ulcer or the aggravation of a previously existing one. Three of these cases were grouped as acute traumatic ulcers, though admitting, correctly, that it is an exceedingly difficult matter to correctly appraise the role which trauma plays as an etiological factor.

In the three cases reported in which trauma was believed to bear a causative relationship, a history of epigastric injury, blood in the vomitus or stool, or both, and X-ray findings constitute the basis for diagnosis. In one case in the group the case was not studied by the author until four months after the injury; during the next eighteen months of observation the clinical and laboratory studies were typical of duodenal ulcer, the question remaining undecided as to whether or not the injury caused the ulcer. In the fifth case there was an antecedent history of digestive disturbance and findings which warranted the diagnosis of a duodenal ulcer, and the injury sustained which constituted the basis of the report was thought to aggravate already existing pathology. The author feels that there can be less controversy concerning the aggravation of pre-existing peptic pathology by trauma than in the group where patients were clinically free of symptoms, but with their development following an injury; even in otherwise fairly clear-cut cases the possibility of the existence of a so-called "silent" ulcer is to be borne in mind.

In his analysis of the symptoms usually observed in such cases Gray lists vomiting as the most frequent symptom and calls attention to the accepted dictum that the danger of gastric injury from external trauma is much greater when the stomach is full. He believes that hematemesis, either in its appearance or its severity, does not furnish a satisfactory criterion as to the extent of stomach damage. The promptness with which a digestive symptom appears following an injury of this sort is emphasized. The author believes that acute traumatic ulcer may result from an external injury, but cautions against too wide acceptance of trauma as a factor by noting the relative infrequency of peptic ulcer following gastric surgery. He looks upon trauma as a factor that rather reveals a pre-existing chronic ulcer than as a factor in the pathogenesis of chronic ulcer formation. The medical legal importance is stressed and a safe rule is laid down when he says that in order to prove that an injury was the cause of a chronic peptic ulcer there should have been X-ray evidence of a normal gastro-duodenal structure done a short time before an accident was sustained; otherwise he believed that the assumption that a chronic peptic ulcer in a given case is due to trauma is entirely speculative.

In connection with the rather large number of cases reported in the German literature, it is interesting to note the author's quotation from Kessler that the German State Insurance Office went on record in 1927, denying that any relationship existed between trauma and gastric ulcer.

Virgil E. Simpson.

JAFFE, R. H., AND LAING, D. R.

Changes in the Digestive Tract in Uremia. Arch. Int. Med., Vol. 53, No. 6, P. 850, June, 1934.

The authors review the literature extensively and cite the various causes of ulceration of the bowel. Treitz believed that urea which is excreted through the glands of the intestinal

mucosa is broken up in the lumen of the intestine into ammonia and carbon dioxide. Ammonium carbonate which exerts a caustic action is formed. Bacterial toxin is given as a cause by Matthieu and Roux.

Pineau offers as his theory of causes, alterations in blood vessels and perivascular tissue, irritation of the nerves and increased blood pressure. Siegmund found arteriolonecrosis in the submucosa in one case of glomerulonephritis and in three of malignant nephrosclerosis. Vollhard stated that in true uremia there is a great tendency to infectious processes, admitting, however, that the role of the toxic action of retained endogenous waste products cannot be completely disposed of. In one hundred thirty-six consecutive cases of uremia that came to autopsy between January 1929 and April 1933, no parallelism was found by the authors between the severity of changes and the duration of the uremic state. In thirty-seven cases (27.1%) the essential change was slight to moderate edema of the submucosa which affected the large intestine. In seventy-two cases (72.9%) hemorrhages occurred in the digestive tract: stomach, ileum, cecum and colon. In eleven cases it was extensive. In twenty-seven cases (19.8%) pseudomembranous and ulcerative changes were found in the esophagus stomach and pleomorphic changes in intestine with intimate relation to hemorrhages of various sizes. None were found in the duodenum. Microscopic examination revealed in mild cases, thickening of the submucosa and dilatation of the veins of the basal venous plexus of the mucosa and submucosa, in hemorrhagic cases extreme congestion of venules and veins, in severe forms complete hemorrhagic infarction of the mucosa, in the state of diphtheritic inflammation completely necrotic mucosa, the necrosis extending into the submucosa. The authors do not accept Treitz' or Siegmund's explanation of the cause of ulceration. No differences in urea retention were found in the mild and severe cases. No arteriolar changes were found in nine of twenty-seven cases of the diphtheritic and ulcerative inflammation of the intestine. They believe that uremic necrosis and ulceration of the intestine are secondary to hemorrhages as Matthieu and Roux suggested.

Leon Bloch.

SAFFER, LOUIS J., AND PAULSON, MOSES.

Residual Hepatic Damage in Catarrhal Jaundice as Determined by the Bilirubin Excretion Test. Arch. Int. Med., Vol. 53, No. 6, P. 809, June, 1934.

Eleven patients were studied at intervals from two months to eighteen years after an attack of catarrhal jaundice, four of whom were symptom-free and five complained of indefinite digestive disturbances at the time of the study. In nine of the eleven the amount of retained bilirubin ranged from ten per cent to fifty per cent, an amount of five per cent being considered of pathologic significance. The severity of the test and the time of occurrence of the jaundice bear no relation to the amount of bilirubin retention. In view of these results it is concluded that catarrhal jaundice is not so innocuous as is commonly believed.

Leon Bloch.

BEER, A.

Haematemasis in Tumors of the Liver. Wiener Klin. Wochenschrift, June 29, 1934.

Case report of melena and hematemasis due to an incomplete obstruction of the portal circulation. The latter was the result of cancer of the gall bladder causing several metastases which involved also the *vena portae*. Such interference of the portal circulation predisposes to stasis in the collateral circulation and any additional factor such as thrombosis in the portal vein may cause a sudden and complete obstruction, resulting in bursting of the oesophageal veins. Also any increase of the intra-abdominal pressure may have the same effect. A compression of the *vena portae* caused by cancer of the gall bladder is not frequently reported in the literature. The absence of splenic tumor is noteworthy and may be explained by the short duration of the pathology. An accompanying prelatal autodigestion of the oesophagus near the cardia also may play a role in producing bleeding from the engorged blood vessels.

M. E. Gabor (Milwaukee, Wis.).

WESTFAHL, K., AND KUCKUCK, W.

Irritable Stomach and Peptic Ulcer. Their Pathology and Therapy. Deutsche Med. z. Woch., 27, 28 and 30, July, 1934.

The preponderance of gastritic components in peptic ulcers is evaluated and analyzed. Gastritis, although a frequent accompanying factor of different types of ulcerations, is *per se* a clinical entity. This has been aptly demonstrated by recent studies gastroscopically, roentgenologically and histologically (on fresh, resected stomachs.) The etiology of gastritis is very complex and the transformation of one type into another is quite common, a hyperacid gastritis changing into an anacid type, etc. It is possible that especially the hyperacid gastritis is a forerunner of peptic ulceration, the latter being a "hemorrhagic, ulcerative" form of gastritis. Other forms of gastritis, namely those lacking gross pathological lesions, are manifested by hyperemia, cellular infiltration, increased activity of the mucous folds. These are functional variations manifested by symptoms closely resembling those of duodenal or stomach ulcers without any pathological findings however. Patients belonging to this category display great sensitivity to normal stimuli and respond with symptoms which the authors divide into two main groups, i. e., hyperergic and hypoergic stomachs. The former occur chiefly in adolescent age and in the more severe cases may show seasonal fluctuation as found in typical ulcerations of the stomach. Estimation of the HCl content is not characteristic. It very often follows some type of infection or may be due to nicotine, etc. The hypoergic variety is concomitant in the asthenic typed individuals especially young people with neurasthenic and "vegetative" stigmata. Subacid and anacid conditions here are often encountered. A cellular exudation combined with congestion and punctal erosion is the result of a sympathetic and parasympathetic instability causing often a circumscribed anemia. The loss of defending epithelium results in an insult of localized areas as manifested by exposure to autodigestion of HCl and pepsin. Irritable stomachs with a hyperergic behavior correspond to vagus while the hypoergic type is analogous to sympathetic irritation. The fully established gastritis is not identical with this syndrome and peptic erosions are not necessarily superimposed upon gastritis. They are, rather, very often the end result of a complicated mechanism consisting of anemic areas which succumb to autodigestion. The degree of HCl content does not seem to be the most important factor.

Therapeutically, we must endeavor to retard leucodiapedesis and an undue increase of HCl formation. Atropin, mild sedatives are given. Alkalies are not recommended but a greater stress is laid upon a well-chosen diet eliminating all such food as may stimulate acid secretion. Any kind of meat belongs to this group as proven by painstaking examination except meat which has been boiled twice. Spinach and the cabbage family are also responsible for a greater stimuli upon the acid secreting glands. On the other hand, fats and oils have the opposite effect inasmuch as they not only retard acid secretion but also reduce a diapedesis of cells thus having a beneficial effect upon capillaries of the mucosa.

M. E. Gabor (Milwaukee, Wis.).

LEMMEL, G.

The Clinical Significance of Diverticula of the Duodenum. Arch. f. Verdauungskrankh, No. 56, July, 1934.

Diverticula of the duodenum are apparently an adjunct of advanced age: in about 10 per cent of all patients over seventy years, duodenal diverticula were found. Their frequency in the sixth or seventh decade seemed to be analogous to the cancer of the stomach. Symptomatology is often vague, at times stormy. It was impossible to establish a clinical entity. The proximity of adjacent tissues especially that of the pancreas and the gall bladder may arouse symptoms characteristic for pathology occurring in these organs. However, to some extent duodenal diverticula may be responsible for complaints that may reveal a more distinct symptomatology, giving rise to the so-called "papilla-syndrome". This consists of phenomena which are due to pathology of the intra- and extrahepatic bile-ducts. Associating pancreatogenous diarrhoeas may occur in parapapillary diverticula. In other cases, sudden colics in the upper abdomen, irrespective of food, may be the results of diverticula situated above the papilla. The incidence of hepatic cirrhosis is mentioned and many cases are treated under this head while the presence of duodenum diverticula is mostly overlooked. In other instances, such diverticula are often considered as and treated for gastric cancer or diseases of the extrahepatic bile ducts. Insufficiency of pancreatic function should always arouse one to the possibility of a duodenal diverticulum. The author purposely disregards etiology and thinks that duodenal diverticula of old age are mostly of the pulsion type. They are often concomitant with the paraoesophageal, hiatua-hernias.

The therapy consists of resection wherever possible, otherwise short-circuiting or duodenal irrigation should be done. The discrepancy between the findings of the pathologists and the roentgenologists is due to the fact that both observers have patients of different ages and ailments for examination.

M. E. Gabor (Milwaukee, Wis.).

CULPEPPER, A. L., AND VON HAAM, E.

Primary Carcinoma of the Liver with Extensive Metastases to the Right Heart, and Tumor Thrombosis of the Inferior Vena Cava. Am. J. of Cancer, 21:355-362, June, 1934.

Primary carcinoma of the liver is not such a rare disease as one might think; the many statistical reports available records its presence in .12 to .14 per cent of all autopsies, and 1.2 per cent of all cancers.

The case here reported is that of a negro, 56 years of age. The antemortem diagnosis was arteriosclerosis with cardiac decompensation. The man died a typically cardiac death.

At necropsy there was edema of the legs with ascites and an

enlarged liver and spleen. The spleen was acutely congested, but the liver contained multiple tumor nodules, and was congested. From the histologic appearance of the growth, a diagnosis of primary carcinoma of the liver was made. Two interesting secondary lesions were found to be the cause of the cardiac symptom-complex. The first of these, and doubtless the first to come during life, was a tumor mass in the right auricle; the second was a metastatic mass producing thrombosis of the inferior vena cava.

As in many other cases of primary carcinoma of the liver, the lesion here found was associated with an early moderate cirrhosis with regeneration of liver cells. This relationship is such a positive one that its significance cannot be lightly regarded. Furthermore, invasion of the vascular channels of the liver, especially the portal radicles, is very common in primary carcinoma of this organ, and the process accounts for the rapid intra-hepatic extension of such tumors. Extension into the hepatic veins and thus into the inferior vena cava has been seen before, but it occurs more frequently with renal and suprarenal tumors.

The tumor implantation in the right auricle was unquestionably blood borne, and resulted from the separation of one of the first bits of tumor to find its way into the vena cava at the point where the tributary hepatic veins enter.

H. J. Wolff (Rochester, Minn.).

CLERF, LOUIS H., AND MANGES, WILLIS F.

The Congenitally Short Esophagus. J. A. M. A., 102:2008 (June 16), 1934.

Atresia of the esophagus with esophagotracheal fistula has been considered the most common congenital anomaly of this structure because of its fatal outcome and opportunity for study at autopsy. Congenital stenosis of the esophagus is not as well known or as frequently recognized, often being confused with the acquired type.

The authors in this paper consider an anomaly characterized by congenital shortening of the esophagus and by the presence in the thoracic cavity of a portion of the stomach, with stenosis at the junction of esophagus and thoracic stomach. There is a scarcity of reports of this condition in the literature. Cases of this type have been improperly diagnosed as acquired stricture and peptic ulcer of the esophagus. The authors report on fourteen cases. The ages in the present series varied from six and one-half years to 32 years.

The symptomatology is divided into two groups. In one group the outstanding symptoms are dysphagia and regurgitation with disturbances in nutrition and growth.

In the second group, distress particularly after eating was an added complaint. The dysphagia dates back to birth or to the addition of solid food to the dietary. In children weight loss is noticeable. The distress may vary from indigestion and flatulence to severe epigastric pain.

GOODALL, HARRY W., AND HOLT, LYMAN H.

Thoracic Stomach. Report of five cases. Vol. 53, No. 4, April, 1934, p. 594.

The authors report five cases of thoracic stomach bringing the total number of reported cases to date up to twelve. They are under the impression that the incidence is higher than is apparent and that the rarity is due to the fact that many of the patients with this condition are probably reported as diaphragmatic hernia. They question the frequency of the occurrence of hernia through the esophageal opening and feel that the roentgenologist has overlooked many cases of thoracic stomach.

The cause of thoracic stomach is ascribed to a failure of normal growth in the length of the esophagus in the course of embryologic development after the stage in which the trachea has already been separated from the esophagus. There may be no symptoms as in Bailey's patient who lived to be 77 or they may be of two distinct types, those referable to embarrassment of the thoracic organs comprising Type I, in which the bulk of the stomach was above the diaphragm, and those which are the result of interference with gastrointestinal mobility with the bulk of the stomach below the diaphragm, comprising Type II. Dysphagia is not a common symptom of thoracic stomach but is of diaphragmatic hernia.

The author believes that thoracic stomach is a definite clinical entity and belongs in the field of internal medicine. Any patient with unmitigated gastrointestinal symptoms with negative routine roentgenological findings should be suspected of having a thoracic stomach. The treatment is entirely palliative.

Leon Bloch.

BROWN, THOMAS R.

Some Notes on Referred Digestive Symptoms. South. Med. Journ., 27:581-586, June, 1934.

The author in an article necessarily general in scope offers an explanation as to why referred symptoms are so common, names the diseases which are most likely to cause confusing symptoms in the digestive tract, and closes his paper with a plea for less narrow specialism in medicine.

The interpretation of abdominal pain is difficult since we do not know its nature or mechanism. This lack of knowledge is evidenced by the numerous explanations offered—change in visceral tonus, spasm, viscerosensory reflex, pain fibers in the splanchnic nerves, compression or stretching of the intrinsic nerves or blood vessels, etc.—none of which is generally accepted.

The potential causes of referred symptoms may be grouped under three headings—the anatomic, the circulatory, and the nervous. The anatomical reason of course results from the close physical proximity of the digestive tract with other abdominal and even thoracic organs. Circulatory causes operate not only by chronic passive congestion due to a failing heart but also by chemical means, secondary to metabolic disturbances and deficient elimination, and by disturbances of infectious or toxic origin. The neurogenic causes are perhaps the most important of all since they are dependent upon both pain and the affectivity of the individual.

Among the diseases to be borne in mind when the patient presents digestive symptoms are social maladjustment, brain tumor, migraine, tabes, acute infections, measles, typhoid fever, diabetes, pulmonary tuberculosis, chronic infectious arthritis, disturbances of the thyroid, pyelitis, pernicious anemia, angina pectoris, etc.

Better histories should be taken, the physical examination should be more complete, and the laboratory used more intelligently, selecting only those tests likely to be of service—instead of utilizing blindly and indiscriminately every known procedure. Definite progress will be made when the case is studied in that manner and the physician recognizes that man is an entity and not a summation of his organs and systems.

J. Duffy Hancock.

POINDEXTER, CHARLES A., AND GREENE, CARL H.

Toxic Cirrhosis of the Liver. J. A. M. A., 102:2015 (June 16), 1934.

The authors point out that chloroform is the best known of the chlorinated hydrocarbons which have a toxic action on the liver. Carbon tetrachloride is closely related chemically to chloroform and is likewise a hepatic poison. It has found wide use in industry because of its non-inflammable character and because it is an excellent solvent for facts and greases.

Acute poisoning from the inhalation of carbon tetrachloride fumes has been recorded. In many of the severe cases, death ensues from an acute toxic necrosis of the liver with the clinical picture of acute yellow atrophy. Experimentally it has been shown that a toxic cirrhosis can be produced in dogs by the administration of small doses of carbon tetrachloride over a long period of time.

The authors report an Italian male, age 46, whose occupation was that of a cleaner of clothes. The cleaning fluid, used in a poorly ventilated room, consisted of a mixture of fifty-five per cent carbon tetrachloride and forty-five per cent naphtha and benzine. There was a negative history for alcohol. The patient developed the clinical picture of cirrhosis of the liver with ascites.

At autopsy the liver showed the picture of chronic hepatitis with cirrhosis.

The authors feel that this case is a counterpart clinically of the experimentally produced lesions in the dog from the use of small amounts of carbon tetrachloride over a long period of time and point out that this case demonstrates that chronic carbon tetrachloride poisoning is an additional industrial hazard.

Francis D. Murphy.

FREEMAN, NORMAN E., AND BROWN, ROBERT L.

Gastric Lavage in the Treatment of Pyloric Obstruction (An Experimental Study). S., G. and O., 58:956-958, June, 1934.

In doing daily aspirations of stomach contents to study the gastric secretion of cats after pyloric obstruction, the authors observed that the animals subjected to repeated lavage survived longer than those which were not so treated. This finding was of interest in view of the work of Gamble and McIver, who believed that death after pyloric obstruction was directly referable to the loss of water and electrolytes from the body by way of the stomach. To check the accidental observation described above, Freeman and Brown carried out a well conceived and controlled experiment, limited, however, to a very small number of animals. Their opinion is that the reduced loss of fluids and chlorides (which accounts for the prolongation of life) is a direct result of keeping the stomach empty—in other words, distention of the stomach has a direct incitant action causing an increased loss of fluids and chlorides from the body by way of the stomach. Protein loss by that route was found to be quite small and the resulting dehydration in pyloric obstruction was not associated with an elevation of body temperature. They suggest that the beneficial effects following the clinical use of gastric lavage in cases of pyloric obstruction is the result of the decrease in the rate of loss of fluids and chlorides.

J. Duffy Hancock.

THE EFFECTS ON GASTRIC SECRETION IN DOGS OF VARIOUS FOOD-SUBSTANCES EMPLOYED IN THE TREATMENT OF GASTRIC ULCER

By

ARMINE ALLEY, M.A.*
MONTREAL, CANADA

THE effect of various "ulcer diets" upon the gastric secretion of the pouch dog has not been investigated in any great detail. It was, therefore, of interest to compare the secretion produced in a gastric pouch on the foods in the diets proposed by Jarotski, Sippy, and Smithies, respectively. Only the simple foods given at the beginning of the ulcer treatment were investigated as those given in the later stages of treatment are of greater variety and, therefore, makes the analysis of their effects in the gastric secretion very complicated.

METHODS

Usually the foods were given by mouth in the manner proposed in the diets and the pure juice collected from a gastric pouch. The investigation of any diet was not carried on for more than one day as the components of these diets, such as butter, milk, cream, and egg-white, may cause a diarrhoea in dogs. Two dogs were used, one (20 kg.) with an Armour pouch (Armour, 1930) formed from the lesser curvature region of the stomach and the other (13 kg.) with a Pawlow pouch formed from the greater curvature region. The gastric juice was analyzed for pepsin by means of Nirenstein and Schiff's modification of Metts' method and for free and total acidity with Topfer's reagent and phenolphthalein respectively. Control experiments were carried out with raw beef-heart at various intervals during the experimental period in order to ensure the normality of the secretory activity of the gastric glands.

Jarotski's (1925, 1926, 1930) diet, consisting of raw egg-white and unsalted butter given separately, was investigated by giving these foods in different experiments. The whole amount of the butter or the egg-white was given by mouth at one feeding as specified by Jarotski. Sippy's (1915) diet consists of small but frequent feedings of equal parts of milk and cream alternating with alkaline powders. In these experiments cream with 15 per cent butterfat or milk with 4 per cent butterfat was given in small amounts either with or without alkaline powders. The cream and the milk were not mixed but were given separately as it was thought that the comparison of their respective effects would be of value. For Smithies' (1917, 1925) diet, consisting of soft carbohydrate gruel, liquid cream of wheat was given, made by cooking 30 gm. cream of wheat in 600 c.c. of water for one-half hour.

The experiments were started when the glands were in a resting condition, i. e. when no secretion or when approximately 0.3 c.c. or less of mucoid secretion occurred in 15 minutes. The Tables have been made from experiments which were considered typical of a repeated number of similar experiments.

TABLE I

Secretion from an Armour pouch on 100 gm. butter and 225 gm. egg-white respectively given in one feeding by mouth or by fistula.

	Expt. 1. Feb. 2.	Expt. 2. Nov. 24.	Expt. 3. Jan. 26.	Expt. 4. Jan. 30.
	Butter 100 gm. by fistula Vols. in c.c. per hour.	*Butter* 100 gm. by mouth Vols. in c.c. per hour.	*Egg-white* 225 gm. by fistula Vols. in c.c. per 15 min.	*Egg-white* 225 gm. by mouth Vols. in c.c. per 15 min.
	0.1 0.2 0.4 0	2.0 0.3 0.2 0.05	0.5 1.0 0.9 0.3 0.1	3.4 1.0 0.5 0.3 0.2 0
Totals	0.7	2.55	2.8	5.4

TABLE II

Secretion from a Pawlow pouch on 100 gm. butter and 225 gm. egg-white respectively given in one feeding by mouth.

Expt. 5, Nov. 24, *Butter*, 75 gm.				Expt. 6, May 5, *Egg-white*, 200 gm.			
Vols. c.c./hr.	Acidity m. eq/l.		Peptic Power	Vols. c.c./hr.	Acidity m. eq/l.		Peptic Power
	Total	Free			Total	Free	
0.8	---	---	---	5.0			
3.0	83	45	635	2.0			
2.8	103	57	200	1.0	128	86	64
3.5	100	65	144	0.3			
6.5	112	66	70	0.2			
4.7	123	61	23	0.1			
Total 21.3	Average 107	Average 60	Average 202	Total 8.6	Average 128	Average 86	Average 64

RESULTS ON JAROTSKI'S FOODS

Table 1 shows that butter and egg-white when given by fistula or by mouth stimulated a very small secretion from the Armour pouch. All the egg-white had passed into the intestine by the end of an hour and a quarter, leaving the stomach in an alkaline (to litmus) resting condition.

It is seen in Table 2 that egg-white stimulated a very small secretion of short duration from a Pawlow pouch which has also been demonstrated by Marbaix (1898), Serdiukoff (1899) and Virshubsky (1900). Butter gave a small but prolonged secretion with a rise towards the end of the secretion which has also been obtained by Piontkowski (1906) on olive oil. The total and free acidities were low, showing a rise to-

*Department of Physiology, McGill University, Montreal.
Submitted July 18, 1934

ward the end of secretion. The peptic power, on the other hand was high at the beginning of secretion but fell continuously to an extremely small figure at the end of the secretion.

In comparing the secretion from the Armour and Pawlow pouches on butter (Tables 1 and 2), a striking difference is seen in the course of secretion and also in the volume, neither of which could be accounted for solely by the greater size of the Pawlow pouch. A four-hour secretion on 100 gm. of butter gave 2.4 c.c. from the Armour pouch while a six-hour secretion on 75 gm. from a Pawlow pouch gave 21.3 c.c. and also displayed a rise in the fourth and fifth hours which did not occur in the Armour pouch secretion.

TABLE III

Secretion on meat by mouth (control) from Armour and Pawlow pouches respectively.

Expt. 7, Dec. 5 — *Armour pouch* 150 gm. beefheart				Expt. 8, Dec. 23. — *Pawlow pouch* 150 gm. beefheart			
Vols. in c.c. per hr.	Acidity m. eq. l. Total	Acidity m. eq. l. Free	Peptic Power	Vols. in c.c. per hr.	Acidity m. eq./l. Total	Acidity m. eq./l. Free	Peptic Power
11.0	158	112	144	16.7	144	107	134
8.2	154	124	144	12.9	146	109	134
4.1	144	99	144	8.1	140	94	138
2.8	110	82	209	3.1	128	88	256
0.6				0.1			
Total 26.7	Average 132	Average 112	Average 151	Total 40.9	Average 140	Average 101	Average 144

In Table 3 are given examples of the control secretions on meat which were obtained from Armour and Pawlow pouches. The courses of secretions in the two pouches were similar and were typical of the normal pouch secretions obtained by Khizhin (1890). The total volumes were different owing to the fact that the Pawlow pouch (6 c.cm. long and approximately 3.5 c.cm. wide) was larger than the Armour pouch (5.5 c.cm. long and approximately 2 c.cm. wide). Since the control secretion of the Armour pouch on meat was normal, the variations from the Pawlow pouch were considered normal for that region of the stomach.

RESULTS ON SIPPY'S FOODS

TABLE IV

Gastric secretion from an Armour pouch after the administration of 600 c.c. of milk or cream by fistula and by mouth respectively.

Expt. No.	Food	Method of administration	Total Volume in c.c.	Average Acidity m. eq./l. Total	Average Acidity m. eq./l. Free	Average Peptic Power	Duration in hours of secretion
9	milk	by fistula	8.8	136	91	27	4½
10	cream	by fistula	3.9	123	96	20	3½
11	milk	by mouth	20.6	154	108	109	4½
12	cream	by mouth	12.2	125	94	35	5

In the experiments 9, 10, 11 and 12 (Table 4), 600 c.c. of milk or cream were given by mouth or by fistula in one feeding to the Armour pouch dog in order to determine the normal secretory activity of the glands. In accordance with Lobassow's (1896) findings, feeding by fistula produced less secretion than feeding by mouth. The pepsin, acidity and duration were also depressed in the fistula feeding.

TABLE V

Gastric secretion on 600 c.c. cream and 600 c.c. milk respectively fed by mouth to an Armour pouch dog in one feeding.

Expt. 12, March 15, *Cream*					Expt. 11, March 7, *Milk*				
Hrs.	Vols. c.c	Acidity m. eq. l. Total	Acidity m. eq. l. Free	Peptic Power	Hrs.	Vols. c.c	Acidity m. eq./l. Total	Acidity m. eq./l. Free	Peptic Power
1	5.6	132	106	43	1	8.6	150	114	103
2	2.4	140	102	40	2	4.6	150	115	40
3	1.7	122	93	30	3	3.3	130	104	37
4	1.5	121	90	27	4	3.0	134	106	62
5	1.1	110	80	30	5	1.3	130	100	100
	Total 12.3	Avr 126	Avr. 99	Avr. 37		Total 20.8	Avr. 143	Avr. 106	Avr. 110

Table 5 gives in detail the results obtained on feeding milk or cream by mouth to Armour pouch dogs. These results vary from the Pawlow pouch secretion in that the first hour was always the highest for both milk and cream.

TABLE VI

Armour pouch secretion on repeated feedings of 600 c.c. cream or 600 c.c. milk in 75 c.c. hourly portions for eight hours by mouth.

Expt. 13, March 9, *Cream*					Expt. 14, March 17, *Milk*				
Hrs	Vols. c.c	Acidity m. eq. l. Total	Acidity m. eq. l. Free	Peptic Power	Hrs.	Vols. c.c	Acidity m. eq./l. Total	Acidity m. eq./l. Free	Peptic Power
1	3.5	138	88	59	1	3.0	130	89	68
2	3.3	134	88	64	2	4.0	135	101	92
3	3.3	142	94	27	3	4.5	138	102	64
4	3.5	138	94	30	4	3.6	140	106	64
5	3.5	136	91	30	5	3.9	140	106	64
6	3.5	134	94	32	6	3.6	142	106	64
7	3.9	136	96	36	7	3.7	142	100	42
8	4.0	137	98	36	8	3.8	141	105	39
	Total 28.5	Avr 137	Avr 93	Avr. 40		Total 30.1	Avr. 138	Avr. 103	Avr. 62

It may be seen from the above experiments (Table 6) that when milk or cream is fed in small and frequent portions the gastric glands of the lesser curvature region produce a small but continuous secretion lasting as long as the food is given. The course of the secretion in an hour following one of the feedings ran approximately as follows in fifteen-minute periods: on cream, in c.c., 1.3, 0.9, 0.7, and 0.6; on milk, 1.6, 1.4, 0.6, and 0.3. It is apparent that the comparatively high secretion at the beginning of each hour is due to the nervous stimulation produced by eating. The total volumes of secretion on cream and milk respectively during the eight hours are quite close (cream, 28.7 c.c., and milk, 30.1 c.c.). This is not the case when the same amounts of cream or milk are given in the one feeding (cream, 12.2 c.c., and milk, 20.6 c.c.) where the secretion on cream is much lower than that on milk and where also the volumes on both milk and cream are lower than when given in repeated feedings. It seems that the inhibition due to the fat in the cream was less effective when the cream was given in small portions. The *acidities* and *peptic powers* of the secretion on repeated feedings of milk and cream respectively *were higher* on the milk. Milk given in *one feeding* produced some of the *highest peptic powers.*

TABLE VII

Gastric secretion on 600 c.c. cream and 600 c.c. milk fed by mouth to an Armour pouch dog in 120 c.c. hourly portions for five hours.

Expt. 15, Nov. 13, *Cream*					Expt. 16, Nov. 17, *Milk*				
Hrs.	Vols. c.c.	Acidity m. eq/l.		Peptic Power	Hrs.	Vols. c.c.	Acidity m. eq/l.		Peptic Power
		Total	Free				Total	Free	
1	2.9	140	89	47	1	4.7	134	91	57
2	2.7	134	80	26	2	4.3	134	87	57
3	2.3	138	88	16	3	4.9	141	74	47
4	2.0	136	84	27	4	3.9	148	80	33
5	2.0	132	82	26	5	4.0	135	95	38
6	1.8	96	63	22	6	2.0	119	71	44
7	1.7	92	76	18	7	1.3	100	60	31
8	1.0	90	50	16	8	0.1			
	Total 18.2	Avr. 125	Avr. 84	Avr. 27		Total 26.1	Avr. 135	Avr. 83	Avr. 47

In experiments 15 and 16 (Table 7), cream and milk were given respectively in equal portions during five hours instead of eight in order to observe the *duration of secretion* after the feeding was stopped. Increasing the fluid fed per hour increased the volume per hour on milk but slightly reduced the volume per hour on cream. A secretion occurred in the sixth, seventh and eighth hours on milk and cream but the volumes were 2.0, 1.3, 0.1, and 1.8, 1.7 and 1.0 respectively.

TABLE IX

Pawlow-pouch secretion on 600 c.c. milk and 600 c.c. cream given in one feeding by mouth.

Expt. 19, May 30, *Milk*					Expt. 20, March 9, *Cream*				
Hrs.	Vols. c.c.	Acidity m. eq/l.		Peptic Power	Hrs.	Vols. c.c.	Acidity m eq l		Peptic Power
		Total	Free				Total	Free	
1	7.0	130	90	202	1	2.0	70	46	220
2	8.9	142	109	16	2	1.7	93	70	64
3	3.8	132	92	85	3	4.0	104	70	30
4	4.9	130	86	144	4	8.1	127	95	9
5	2.8	120	80	188	5	8.7	132	104	9
6	1.0	112	60	225	6	7.7	137	99	16
					7	7.0	129	95	16
					8	6.7	127	92	20
					9	4.5	120	90	18
	Total 28.3	Avr. 133	Avr. 91	Avr. 118		Total 53.4	Avr 105	Avr. 90	Avr 27

After giving milk in one feeding (Table 9) the curve of secretion was highest in the second hour which is followed by a rapid drop in volume and a slight rise in the fourth hour. Cream fed in this manner stimulated a gradual *increase in secretion* which remained high until the eighth hour, after which there occurred a fall. Thus on the increase of fat in the fluid food given, the hourly volumes at the beginning of the secretion were depressed, those toward the end

TABLE VIII

Gastric secretion from an Armour pouch on 600 c.c. cream fed by mouth in 100 c.c. and 50 c.c. alternating portions with or without alkali respectively every half hour for four hours.

Expt. 17, March 24, *Cream* (Control)					Expt. 18, March 22, *Cream and Alkali*				
Procedure	Vols. in c.c. per ½ hr.	Acidity m. eq. l.		Peptic Power	Procedure	Vols. in c.c. per ½ hr.	Acidity m. eq./l.		Peptic Power
		Total	Free				Total	Free	
100 c.c. cream	2.0	138	98	48	100 c.c. cream	2.7	134	96	50
50 c.c. cream	1.9	138	98	32	50 c.c. cream + "A"	5.2	151	106	25
100 c.c. cream	2.0	142	90	30	100 c.c. cream	4.5	142	106	15
50 c.c. cream	2.4	141	97	30	50 c.c. cream + "B"	4.3	153	122	16
100 c.c. cream	2.9	140	100	21	100 c.c. cream	3.4	151	122	6
50 c.c. cream	1.7	138	98	17	50 c.c. cream + "A"	1.2	152	116	6
100 c.c. cream	2.1	138	94	15	100 c.c. cream	2.0	134	104	9
50 c.c. cream	1.1	132	93	20	50 c.c. cream + "B"	1.9	142	118	6
	Total 16.1	Avr. 139	Avr. 96	Avr. 27		Total 25.2	Avr. 146	Avr. 111	Avr. 18

Powder "A" = 0.6 gm. $NaHCO_3$ and 0.6 gm. heavy calcined magnesia.
Powder "B" = 2 gm. $NaHCO_3$ and 0.6 gm. $CaCO_3$.

In experiment 18 (Table 8) where alkaline powders (original Sippy's dose) were given, the *total secretion was greater* than that obtained on cream alone fed in a similar manner as in experiment 17. It was necessary to give some cream with the alkali as the dog refused the powders in pure water. The first dose of alkali decidedly increased the secretion but each succeeding dose seemed to have less effect. The *acidity was decidedly increased* every time the alkali was given and the peptic power decreased throughout the secretion.

PAWLOW POUCH SECRETION ON THE FOODS GIVEN IN A SIPPY DIET

The experiments carried out on the Armour pouch dog were repeated on a Pawlow pouch dog in a similar manner. The activity of the greater curvature region may be considered more representative of the activity of the body of the stomach. In certain respects this greater curvature region showed striking differences in reaction to the Sippy-diet foods as compared with the lesser curvature region.

increased and the duration of the secretion lengthened. Increasing of the fat also, on the whole, decreased the acidity and especially the peptic power. It will be noticed that the acidity and peptic power do not follow similar courses, and the increase in acidity tends to follow the increase in fluid.

In the next set of experiments (Table 10) both the cream and the milk were fed in 100 c.c. portions for six hours. The secretion on cream was collected for nine hours and that on milk for eight. The total volume on cream (56.9 c.c.) for eight hours showed only a small increase over that on milk but the secretion on milk had practically stopped in the eighth hour, whereas cream produced 7.4 c.c. in the ninth hour at the end of which the flow of juice was still copious. The total volume of both the cream and milk fed repeatedly is greater than when they were given in one feeding. The *increase in the secretion* in the second half of the secretory period is also much *higher than when food is given in one feeding.* This difference may be due to the repeated nervous stimulation (indicated by the act of eating), and possibly also to the greater rise in

TABLE X

Gastric secretions on feedings of 600 c.c. cream or 600 c.c. milk given in 100 c.c. portions for six hours by mouth to a Pawlow-pouch dog.

Expt. 21, March 21. Cream					Expt. 22, April 3. Milk				
Procedure	Vols. in c.c. per hour.	Acidity m. eq/l. Total	Free	Peptic Power	Procedure	Vols. in c.c. per hour.	Acidity m. eq/l. Total	Free	Peptic Power
100 c.c. cream	2.5	94	52	150	100 c.c. milk	4.3	122	85	400
100 c.c. cream	3.5	114	83	49	100 c.c. milk	5.7	131	80	144
100 c.c. cream	4.5	121	86	50	100 c.c. milk	6.5	131	92	94
100 c.c. cream	5.9	122	85	10	100 c.c. milk	8.2	141	100	68
100 c.c. cream	8.1	131	98	14	100 c.c. milk	8.8	141	102	77
100 c.c. cream	11.1	140	104	11	100 c.c. milk	9.3	140	98	36
	10.0	138	104	16		3.0	131	88	131
	11.0	137	90	16		1.5	118	84	243
	7.4	132	92	16					
	Total 65.3	Avr. 132	Avr. 91	Avr. 25		Total 47.3	Avr. 136	Avr. 94	Avr. 116

volume towards the end of the secretion. On comparing the peptic powers and acidities of milk and cream fed in repeated small portions, the *acidity is on the whole slightly higher* and the *peptic power decidedly higher on milk.* The courses of the peptic power and acidity do not run parallel to each other with either milk or cream. The acidity tends to rise or fall with the increase and decrease of fluid while the peptic power starts high with both milk and cream, then falls considerably, followed by a rise on milk only.

TABLE XI

Gastric secretion on 600 c.c. of cream fed to Pawlow-pouch dog, 100 c.c. every hour for six hours with alkali given halfway between the hourly feedings by mouth.

Expt. 23 May 22	Vols. in c.c. per ½ hr.	Vols. in c.c. per hr.	Acidity m. eq/l. Total	Free	Peptic Power
100 c.c. cream	2.1	6.2	106	56	410
Powder "A"	4.1		130	90	117
100 c.c. cream	2.5	7.0	128	95	16
Powder "B"	4.5		131	104	9
100 c.c. cream	3.1	7.1	125	97	16
Powder "A"	4.0		127	86	16
100 c.c. cream	3.6	8.9	130	91	16
Powder "B"	5.3		132	102	16
100 c.c. cream	3.9	11.9	136	108	25
Powder "A"	8.0		142	104	14
100 c.c. cream	7.5	15.2	142	108	25
Powder "B"	7.7		143	114	14
	7.7	11.5	146	118	15
	6.8				
	5.7	11.5	138	106	16
	5.8				
	5.2	9.3	136	104	20
	4.0				
	Total 94.6	Total 94.6	Avr. 138	Avr. 104	Avr. 43

Powder "A" = 0.3 gm. heavy calcined magnesia and 0.3 gm. $NaHCO_3$
Powder "B" = 1 gm. $NaHCO_3$ and 0.3 gm. $CaCO_3$

When alkali (half Sippy's dose) was given halfway between the hourly cream feedings, as in experiment 23 (Table 11), the *total volume secretion in nine hours was increased* (63.3 c.c. and 90.6 c.c. respectively) as compared with the volume obtained when the cream was given without the alkali (Expt. 21). The dog tolerated the alkali when it was dissolved in 30 c.c of water to which were added three drops of cream. After *each* dose of alkali there occurred *not only an increase in volume but also an increase in acidity.* The peptic power did not seem to be affected by this amount of alkali and remained at a constant low level.

RESULTS ON SMITHIES' FOOD

In Smithies' diet small amounts of liquid gruel are administered repeatedly. In the present investigation, however, 500 c.c. of liquid cream of wheat was given to a Pawlow pouch dog at one feeding in order to determine the duration and volume of secretion without repeated nervous stimulation. The cream of wheat was prepared by cooking 30 gm. of the dry substance in 600 c.c. of water.

TABLE XII

Secretion of a Pawlow-pouch on giving 500 c.c. cream of wheat (Smithies) in one feeding to the dog by mouth.

Expt. 24, March 21.				
Hrs.	Vols. c.c.	Acidity m. eq/l. Total	Free	Peptic Power
1	0.1	130	85	91
2	2.5	97	61	441
3	2.1	96	56	607
4	1.9	83	48	607
5	2.0	81	45	753
6	1.9	85	37	499
7	0.9			300
	Total 17.4	Avr. 100	Avr. 63	Avr. 391

The results in experiment 24 (Table 12) show the normal carbohydrate effect in the gastric glands where the secretion is very small and of prolonged duration with *very low acidity* and *high peptic power* (Khizhin, 1890). The *total volume was low,* being less than that on 600 c.c. of milk. No mucus was secreted in the first hour, but in the hours following visible mucus made up approximately .5 c.c. of the volume secreted.

TABLE XIII

Effect of 500 c.c. cream of wheat on gastric secretion of a Pawlow-pouch produced by 75 grams of fat, both foods given by mouth.

Expt. 25 May 9.	Vols. c.c./hr.	Acidity m. eq/l. Total	Free	Peptic Power	Expt. 26 May 11.	Vols. c.c./hr.	Acidity m. eq/l. Total	Free	Peptic Power
Butter	0.8	---	---	---	Butter	0.6	---	---	---
	1.6	52	32	243		1.9	48	32	433
	1.0	60	36	144		2.0	52	32	196
	3.1	90	52	100	Cream of wheat	3.4	85	56	144
	4.0	100	76	42		4.4	108	76	77
	2.4	86	68	36		2.0	84	60	30
						0.2	---	---	---
	Total 12.9	Avr. 85	Avr. 59	Avr. 91		Total 14.5	Avr. 89	Avr. 56	Avr. 161

In experiment 26 (Table 13) the carbohydrate stimulus was superimposed upon the secretion on fat in

order to see if the carbohydrate had any effect on the secretion on fat or vice versa. The cream of wheat was given at the beginning of the fourth hour of the fat secretion, the hour during which there is a noticeable rise in secretion accompanied by a *rise in acidity and fall in peptic power*. In comparing experiment 26 with its control (Expt. 25, Table 13) it will be seen that volumes, acidities and peptic powers do not vary in any significant degree in spite of the fact that 500 c.c. of liquid cream of wheat was given at the beginning of the fourth hour.

One further type of experiment was carried out in order to investigate the neutralizing effect the cream of wheat has on the gastric juice of *vivo*. Three control experiments were performed in which a dog with oesophagotomy and gastric fistula was shamfed with minced beefheart for five minutes. Averages were taken of the total volume (127 c.c.) and acidity (total 148 and free 103 obtained) in the first three-quarters of an hour in these experiments. In other experiments fifteen minutes after the usual sham feeding with meat, liquid cream of wheat was fed to the animal and then administered down its oesophagus by means of a rubber tube (usual method of feeding). The stomach contents were drained at the end of three-quarters of an hour from the time of sham feeding and tested for free and total acidity. On giving 300 c.c. of liquid carbohydrate there was *no free acidity* and the *total acidity was only 24 m.* eq/l. the 200 c.c. of stomach contents obtained.

DISCUSSION

In the above results it is seen that the lesser curvature region reacted differently from the greater curvature region on diets which had fat as a component, although both their reactions to meat as a control were similar. This was demonstrated both with the butter of Jarotski's diet and with the cream of Sippy's diet. On both these foods the secretion from the Armour pouch was small while that from the Pawlow pouch, although scanty at first, increased to considerable volumes in the later hours of secretion.

The Armour pouch, since it is formed in part from the lesser curvature region, probably does not give a true picture of the major secretory activity of the stomach on certain food substances, such as fat. Thus the results from the Pawlow pouch give probably more complete information in regard to the effect of the foods in the diets. However, since ulcers occur more frequently in the lesser curvature region, it is of interest to know the kind of secretion produced there.

The effect of the gastric secretion of different methods (by fistula, in one feeding by mouth and in repeated feeding by mouth) of feeding milk or cream will now be discussed. Milk or cream fed by fistula to the Armour pouch dog produced less secretion with lower acidity and lower peptic power than when fed by mouth (demonstrated also by Pawlow in his pouch dog). Repeated feedings of small amounts of milk or cream by mouth produced a continuous secretion from both Armour and Pawlow pouches, due presumably to a continuous nervous stimulation. If this secretion is compared with that obtained when the same amount is given in one feeding, the most striking fact is that the former shows an increase in volume over the latter. In feeding by these two methods the courses of pepsin and acid were fairly similar for cream and milk respectively, i. e., the course on milk for peptic powers for both the methods was high at the beginning and end, while the lower volumes produced in between were greater in number on the repeated feeding method.

When the alkali in whole Sippy's or half Sippy's doses was added to the repeated feedings, the *fluid and acidity of the secretion were increased* in both Armour and Pawlow pouches. The pepsin did not seem to be affected except in the Armour pouch secretion in which it was depressed. It has been shown by Browne and Vineberg (1932) that an increase in the CO_2 content in the blood can stimulate the gastric secretion.

In comparing the respective effects of milk and cream on the gastric secretion, it was found that *milk produced a greater secretion with higher peptic power and acidity* with all types of feeding in an Armour pouch dog. In the Pawlow pouch dog there was always a much *lower peptic* power and *slightly lower acidity*.

From the experiments carried out on the above foods it is seen that Sippy's diet, as it consists of repeated feedings of cream, kept the gastric glands in an *active secreting state* producing a juice with moderate acidity and low peptic powers, not only during the period of feeding but for a prolonged period after the feeding was stopped. This prolonged secretion was not seen on milk. Alkali added to the cream feedings *increased the acidity and volume*, although it tended to lose its effect in the later hours of the Armour pouch secretion. The protein of Jarotski's diet given in the form of egg-white stimulated a small secretion of low acidity and peptic power. Butter, on the other hand, stimulated secretion like that produced by cream but much smaller in amount and less prolonged. The cream of wheat in Smithies' diet produced a secretion which, although *low in volume and acidity*, had a *high peptic power*.

Cream of wheat was given during the secretion on butter, and its effect on the glands (high peptic power, etc.), believed to be almost entirely nervous (Pawlow, 1910), was apparently completely inhibited and the secretion on butter lasted only fifteen minutes longer than the control. Other experiments showed that this carbohydrate greatly reduced the acidity of the gastric secretion. From this it might be suggested that cream of wheat given during the peak of the secretion on butter does not produce its usual secretion with a high peptic power and probably neutralizes the increased acidity of the butter secretion during that period. It also increased the caloric value of the diet and may also serve to supplant some of the butter if the fat is eaten with difficulty.

SUMMARY

The effects on the gastric secretion in two pouch dogs, of some of the foods in Jarotski, Sippy, and Smithies' diets were investigated with the following results:

1. Cream or milk fed repeatedly produced a continuous secretion, and that on cream was much more prolonged than that on milk, but the peptic power on milk was higher. Alkalies increased the volume and acidity.

2. The volumes of secretion on milk or cream were much greater when given repeatedly as compared to those in one feeding.

3. Egg-white and butter produced comparatively small secretions.

4. Cream of wheat stimulated a small secretion of high peptic power and low acidity which was entirely inhibited when given during the peak of butter secretion. Liquid cream of wheat has the power of completely neutralizing the free acidity and greatly reducing the total acidity of sham feeding juice.

5. Differences of secretory behavior were noticed between the glands of the greater curvature and lesser

curvature regions in that the foods containing fat produced in the former a secretion greater in volume and longer in duration than in the latter.

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A NOTE ON THE RÔLE OF ACHLORHYDRIA IN THE ETIOLOGY OF SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD*

AN EXPERIMENTAL STUDY IN THE GASTRECTOMIZED DOG

By

A. C. IVY, Ph.D., M.D., F. P. CUTHBERT, M.S., B.M.

and

A. WEIL, M.D.

CHICAGO, ILLINOIS

REPEATEDLY, it has been claimed that the absence of free hydrochloric acid in almost 100 per cent of cases of subacute, combined degeneration of the spinal cord plays an important role in the etiology of that affection. One of us (A. W.) together with Davison (1) and others have pointed out that achlorhydria may also be found in a number of normal persons who never develop spinal cord disease and that probably achlorhydria rather is a *sequela* than a causative factor in the course of a disease which may result either in subacute combined degeneration of the spinal cord, or pernicious anemia or both.

The following experiments on dogs support those conclusions which had been derived from human material. In four dogs, gastrectomies were performed which the animals survived for periods lasting from three and one-half to eight and one-half years. Either the stomach was entirely excised or a pouch of the entire stomach was made with a duodeno-esophageal anastomosis.

In the first instance (No. 10) a complete gastrectomy was done and the dog survived for seven years and two months without ever developing anemia. During the last six months a carcinoma of the thyroid developed which *at autopsy* was found to have metastasized to the lungs, spleen and lumbar vertebrae. In the last region, extradural metastases had compressed the spinal cord and produced a myelopathy, which, on superficial examination, might have been mistaken for a beginning subacute combined degeneration. The remainder of the spinal cord did not show any pathologic changes.

In the second dog, a pouch of the entire stomach had been formed. He survived eight years and ten months. Three short periods of a transitory, secondary anemia lasting one month or so were observed in this dog (RBC, 3.5 millions, Hgb., 9.5 grams), which disappeared following the administration of iron and, the last time, by treatment with liver extract. He died of pneumonia. *At autopsy* the stomach pouch was found to be very small and thick-walled; no ulcers or erosions were seen; the esophago-jejunal junction was slightly dilated. There was a marked atrophy of the spleen. The periphery of the lower dorsal, spinal cord showed a mild edema without, however, any destruction of myelin sheaths or of glia proliferation. This process was considered to be of an acute nature, perhaps in connection with the final pneumonia.

The third dog survived four and a half years the formation of a pouch of the entire stomach. He was never anemic. He died with the symptoms of an acute encephalitis. *At the autopsy*, no hypertrophy or dilatation of either esophagus or duodenum at the site of the anastomosis was found. The spleen was markedly enlarged; in the center of a necrotic lymphoma, serous material was observed. Both kidneys were very small and atrophic. The histologic examination of the spinal cord revealed in the upper cervical segments a mild acute poliomyelitis with scattered perivascular hemorrhages, scanty perivascular small round cell infiltra-

*From the Department of Physiology and Pharmacology, and the Institute of Neurology, Northwestern University Medical School.

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(1) A. Weil and Ch. Davison. Changes in the spinal cord in anemia. *Arch. of Neurol. and Psych.*, 22:966; 1929.

tion and glia proliferation. The remainder of the spinal cord was not involved; no changes in the form of a subacute combined degeneration were present.

The fourth dog died from an accident three and a half years after the formation of a pouch of the entire stomach. The dog had been followed through three pregnancies, during each of which the red blood cells diminished approximately from 17 to 40 per cent, the hemoglobin from 20 to 35 per cent. Two weeks following parturition the blood picture had returned to normal. *At the autopsy* the histologic examination of the spinal cord did not show any pathologic changes.

SUMMARY

The spinal cords of four dogs rendered achlorhydric for from three and one-half to eight and one-half years by gastrectomy or direct duodeno-esophageal anastomosis were examined. Subacute combined degeneration of the spinal cord was not demonstrable when the animals were autopsied.

ABSTRACTS

McLAUGHLIN, CHARLES W., JR., AND LEVERING, J. WALTER.

The Effects of Increased Intragastric Pressure upon Thoracic and Abdominal Arterial and Venous Pressures. Surgery, Gynecology and Obstetrics. Vol. LVIII, No. 4, April, 1934, pp. 699-705.

The authors state that gastric dilatation is a progressive lesion which in its earlier stages can be demonstrated by X-ray, by percussion, or by the stomach tube. The mechanism of the production of gastric dilatation, the effect of fluid loss on the circulating blood, and the effect of salt loss on the blood reaction have been discussed at great length in the literature. Little has been written concerning the effect of intragastric tension on the vascular system.

The authors believing that changes in the gastric tension may have profound primary effects on the cardiovascular system have investigated that point in dogs. The dogs were anaesthetized with sodium amytal (50 mg. per kg.). A tube was introduced into the stomach through the esophagus. A high midline abdominal incision was then made and the tube fastened in place at the cardia; the pylorus was firmly closed with stout ligatures and the abdomen closed. Canulas were then placed in the carotid and femoral arteries, the inferior vena cava through the femoral vein, and into the thoracic veins through the external jugular vein. Pressure changes in the veins were measured by means of a one-millimeter bore straight manometer filled with 6 per cent sodium citrate. The gastric tube was connected with a mercury manometer by means of a side arm. All pressures and the pulse rate of the animal were recorded on a kymograph. The animals were kept in the supine position. All experiments were of the acute type; the animals were sacrificed at the conclusion of the experiment.

It was found that pressure in both vanae cavae rose in direct proportion to the intragastric tension. An intragastric tension of 150 mm. hg. was accompanied by a pressure of 300 mm. of citrate solution in the inferior vena cava, and by a pressure of 30 mm. of citrate solution in the superior vena cava.

Pressure in the femoral artery fell until the intragastric tension rose to 50 mm. hg. when as a rule it began to rise, and continued to rise until intragastric tension reached 70-80 mm. hg. When the femoral pressure rose the pulse pressure decreased, and when the gastric pressure was increased above 60 mm. hg. the mean femoral pressure frequently rose from 10-15 mm. above the initial pressure.

Increasing intragastric tension to 110 mm. hg. or above, frequently caused a sudden drop in the femoral pressure to approximately the initial mean pressure or lower than this while the pulse pressure disappeared.

Pressures in the carotid artery did not always parallel those in the femoral artery. With intragastric pressures of from 30 to 50 mm. hg. there was a fall in the carotid pressure. Increasing intragastric tension above 60 mm. hg. resulted in a rise in carotid pressure to its original level. Further increase in intragastric pressure was accompanied by a rise in carotid pressure above its initial level and an increase in pulse pressure while the femoral pulse pressure disappeared. As intragastric pressure was suddenly released the carotid pressure fell to 10 to 15 mm. hg. below its original level. It rapidly returned to normal however.

The authors deduce that the changes in pressure in the venae cavae are due to mechanical obstruction of the vena cava superior by the distended stomach causing increased pressure distal to the obstruction and causing a greater inflow of blood through the vena cava superior by opening the anastomoses between it and the vena cava inferior. The fall in carotid and femoral pressures may be explained on the reduced amount of blood available for the circulation. The rise in arterial tension which accompanied intragastric tensions of 60 mm. hg. or more may in part have been due to vasoconstriction in the head, neck, and upper extremities, and to arterial blood carried to the inferior arterial circulation through vertebral anastomoses, and to venous blood being carried from the inferior to the superior circulation.

The sudden disappearance in femoral pulse pressure was probably due to arterial tamponade due to the greatly distended stomach. The increase in carotid pulse pressure observed during this period may have been the result of mechanical factors causing an alteration in the dynamics of the superior circulation. At this time the respiration is embarrassed by the greatly distended stomach which causes a fixation of the lower portion of the costal arch. The aortic and carotid sinus reflexes play no part in the mechanism because it has been observed when the vagi were divided and the carotids ligated.

The rapid return of arterial and venous pressures to their original levels when gastric distention which had been maintained for only a short period was released, is good reason for the early relief of gastric dilatation in the human.

The reduction of blood volume, loss of fluid and disturbance of acid base balance together with these disturbances in the circulation of the blood make it of great importance to prevent any increase in intragastric tension. The authors recommend continuous gastric syphonage as suggested by Paine, Carlson and Wangensteen.

Nelson M. Percy.
R. H. M. Hardisty.

ALLEY, A.

Excitatory and Inhibitory Effects of Histamine on the Gastric Secretion. Trans. Roy. Soc. of Canada, Vol. 28:126, 1934.

It was demonstrated on dogs with a Pawlow or an Armour pouch and on dogs with oesophagotomy and a gastric fistula that the secretory effect of a standard meal or of sham-feeding was greatly diminished if these were given immediately after the cessation of a preceding gastric secretion stimulated by injection of histamine. The inhibitory effect of histamine was not due to the loss of fluid with the gastric juice, because repeated injections of histamine gave the same volume of secretion, and a secretion activated by sham-feeding or a standard meal was not diminished if pilocarpin had been previously administered. Therefore it seems that histamine, being itself a stimulant of gastric secretion, inhibits the secretory effect of other stimuli which act chiefly through the parasympathetic nervous system.

B. P. Babkin (Montreal, Canada).

KOMAROV, S. A.

Isolation of Mucoitin-Sulphuric Acid from Dog's Gastric Juice. Trans. Roy. Soc. of Canada, Vol. 28:126, 1934.

A substance having all the properties of mucoitin-sulphuric acid was isolated from the products of alkaline hydrolysis of freshly secreted, filtered gastric juice obtained from dogs with gastric fistula and oesophagotomy by sham-feeding. This finding gives a strong support to the previously expressed supposition that a mucin is present in solution in the pure gastric juice.

B. P. Babkin (Montreal, Canada).

SECTION III—*Nutrition*

CLINICAL TYPES OF HYPERINSULINISM

REPORT OF CASES*

By

SEALE HARRIS, M.D.
BIRMINGHAM, ALABAMA

HYPERINSULINISM, *i. e.*, the spontaneous, excessive secretion of insulin by the islands of Langerhans of the pancreas, now recognized as a definite disease entity, is perhaps as frequent a condition as the opposite condition, hypoinsulinism (diabetes mellitus), in which there is deficient secretion of insulin (Harris[1]). A number of cases of hyperinsulinism have been reported in which the important symptoms were neuroses, including headaches (Winans[2]), nervous indigestion (Sippe and Bostock[3]), tachycardia (Waters[4]), angina pectoris (Sippe[5]), hysteria (Heyn[6]), mild and grave epileptiform attacks, including mental lapses and convulsions (Powell[7]), and certain forms of the psychoses (Graham[8]).

Since hyperinsulinism was recognized, described and named in 1923,[9] many cases have been reported by a number of American and European clinicians;[10] (Gammon and Tennery,[11] Wauchope,[12] Sigwald[13]); there can be no doubt but that the condition is a frequent one, and is not recognized up to this time because physicians have not been looking for it. Cammidge,[14] an English clinician, reported 200 cases with low blood sugar readings in which there were definite symptoms of hypoglycemia. Cammidge believes, however, that the liver is a more important factor than is the pancreas in the etiology of his cases of spontaneous hypoglycemia.

In the last eleven years—up to September, 1934—I have studied 112 cases of unmistakable hyperinsulinism, in which the symptoms definitely were due to spontaneous hypoglycemia apparently resulting from the excessive secretion of insulin by the pancreas. Blood sugar studies on all these patients have shown low readings. A number of these cases were diagnosed as hyperinsulinism by other physicians and sent to me for treatment; and in others the diagnosis was not suspected until low, fasting blood sugars were found in the routine laboratory examination of patients, whereupon careful questioning elicited unmistakable symptoms of hypoglycemia.

CLINICAL TYPES OF HYPERINSULINISM

Since many cases of hyperinsulinism have been reported in the last eleven years by a number of capable American and European observers, sufficient data have accumulated from which to classify the protean symptoms of spontaneous insulinogenic hypoglycemia into three clinical types, i. e., (1) mild, (2) moderately severe, and (3) severe hyperinsulinism. In the last named group may be classed the cases in which there are recurring attacks of unconsciousness with, and without, convulsions.

1. *Mild Type:* The patient having mild hyperinsulinism presents the *bizarre* symptoms frequently observed in diabetics from overdoses of insulin. He becomes pale, particularly around the lips, and has various nervous symptoms, particularly those usually classed as anxiety neuroses. Weakness is usually pronounced, and frequently there are trembling and sweating. All the symptoms of mild hyperinsulinism subside in a few minutes after taking soluble carbohydrates, such as orange juice or sugar, and the patient usually is comfortable for three or four hours after meals. In such cases, the blood sugar levels when fasting or during the attacks usually range from 0.075 to 0.065 per cent milligrams.

2. *Moderately Severe Type:* In the moderately severe type the symptoms of the mild type are exaggerated, i. e., there is prostration, and the anxiety neuroses are more pronounced. There are profuse perspiration, sometimes mental lapses, perhaps brief periods of unconsciousness, and spasms of groups of muscles as in *petit mal*. In this type the fasting blood sugar, or in from 4 to 6 hours after the ingestion of dextrose (1½ grams of body weight), usually ranges from 0.065 per cent to 0.055 per cent. The hypoglycemic symptoms of the moderately severe type are relieved in a few minutes after taking soluble carbohydrates.

3. *The Severe Type:* In the severe cases of hyperinsulinism there are recurring attacks of unconsciousness and convulsions, often resembling narcolepsy or the *grand mal* seizures of epilepsy. Manifestations of major hysteria and actual psychoses have been observed in a number of cases. In this type the hypoglycemia is pronounced, the blood sugar readings ranging from 0.055 per cent downward—in Weil's[15] case to zero. It should be remembered, however, that the severe manifestations of hyperinsulinism may be found with blood sugar readings only slightly below normal, as in the cases of "epileptiform convulsions" reported by Neilson and Eggleston[16] with blood sugar readings of 0.067 and 0.069 per cent. Likewise low blood sugar readings have been reported in patients who had no symptoms of hypoglycemia.

While there have been many excellent studies on hyperinsulinism by a number of capable clinicians and pathologists, there is much to learn about this new disease entity, which appears to be relatively as impor-

*From the Medical Division, the Seale Harris Clinic.
Submitted September 11, 1934.

tant as hyperthyroidism, hyperpituitarism and hyperadrenalinism, conditions which have been proved to be due to the hyperactivity of other organs of internal secretion.

The symptoms, diagnosis and treatment of three types of hyperinsulinism may be brought out best by reporting a few cases of each variety.

CASE REPORTS OF MILD HYPERINSULINISM

Cholecystitis, Probable Pancreatitis and Hyperinsulinism. Case 1. H. J. R. Birmingham, Ala. Laborer, Age 67. Height 5 feet 10½ inches. Weight 151 pounds. Has been under observation for 17 years. In 1917 he had diarrhoea, passing mucus and blood, then diagnosed as colitis. Recurring attacks of abdominal pains, chronic indigestion—chronic cholecystitis suspected. Symptoms of hyperinsulinism recognized in 1923.[1] He then complained of attacks of extreme hunger, weakness, nervousness, trembling and profuse perspiration before the noon and evening meals and at night. Symptoms more pronounced if meals are delayed or if he works hard. Symptoms relieved by eating. The hyperinsulinism symptoms have been controlled and prevented by dieting. He "craves sweets" and occasionally will break his diet and eat excessively of candies and desserts. The hypoglycemic symptoms always become more pronounced after a "sugar spree". Has had recurring attacks of abdominal pain, tenderness in upper abdomen over the gall bladder and pancreas, nausea and vomiting. Graham-Cole test showed non-functioning gall bladder. Chronic pancreatitis suspected. Operation has been advised repeatedly but refused each time.

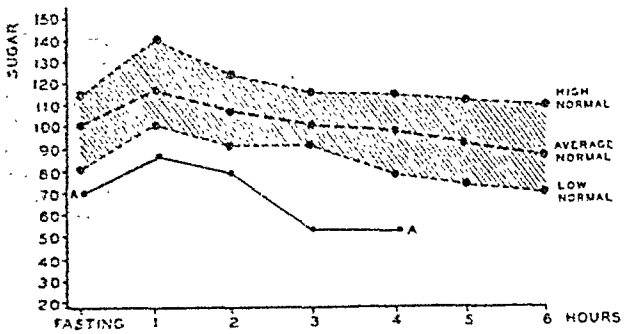


Chart 1. Case 1. A. Glucose tolerance curve, 1931.

COMMENT: The etiological factors in this case seem to have been the colitis and the cholecystitis, with secondary infection of the pancreas. A cholecystectomy years ago might have prevented the hyperinsulinism. An exploration now seems advisable and if the symptoms grow worse the patient likely will submit to the operation. The incidence of gall bladder disease, gall stones and diabetes mellitus is well known, and enough cases of hyperinsulinism associated with cholecystitis and cholelithiasis have been reported to establish their relationship.

Hyperinsulinism and Duodenal Ulcer. Case 2. C. L. M. Natchez, Miss. Steamboat pilot. Age 27. Height 5 feet 9½ inches. Weight 144 pounds. Symptoms: Gnawing, burning pain in stomach when empty, relieved by eating. Tender spot in abdomen 6 c.m. above and to right of umbilicus. Is very nervous, hands tremble, and he becomes exhausted physically if meals are delayed. Eats between meals to relieve pain and prevent weakness. Insomnia the latter part of the night due to hunger pain, weakness and nervousness. Laboratory findings: Wassermann, negative. Fasting blood sugar 0.066 per cent. In making gastro-intestinal X-ray series six hours after barium and malted milk, his blood sugar was 0.050 per cent. His glucose tolerance test was as follows: Fasting, 0.060; 1 hour, 110; 2 hours, 85; 3 hours, 70; 4 hours, 60; 5 hours, 60; the glucose tolerance test was discontinued at the end of 5 hours when his blood sugar was 0.060 per cent because the symptoms of extreme weakness, nervousness and abdominal discomfort were so pronounced that a glass of malted milk was given for relief. The symptoms subsided in a few minutes. Examination of gastric contents showed hyperchlorhydria. Occult blood in stools. X-ray showed filling defect in duodenum.

Treatment and Result: Rest in bed for 3 weeks. Modified low carbohydrate, high fat ulcer diet, with frequent feedings, relieved symptoms immediately. No symptoms of ulcer or hyperinsulinism in two years. Has gained 30 pounds.

COMMENT: This patient undoubtedly had a duodenal ulcer and hyperinsulinism. It seems probable that the infection which caused the ulcer was the etiological factor in a pancreatitis which resulted in hypersecretion of insulin. Rapid eating, with irregular meals, a diet deficient in vitamins, and chronic fatigue from long hours and overwork were considered predisposing etiological factors. A diet rich in vitamins, with frequent feedings, rest, and correction of the patient's living habits seem to have cured both the ulcer and the hyperinsulinism.

Achlorhydria and Hyperinsulinism. Case 3. J. D. C. Charleston, Miss. Minister. Age 26. Height 6 feet 1½ inches. Weight 158½ pounds. Symptoms: Complains of weakness, trembling, nervous sensations and discomfort in stomach coming on when stomach is empty—just before meals and usually about 4 or 5 p. m. Is very hungry at these times and is relieved by taking food. Has weak trembling spells nearly every morning. Has difficulty in concentrating his mind on his duties and at times has slight dizzy attacks. In 1928 was examined in Nashville and sugar found in urine. Was told that he had a tendency towards diabetes and his carbohydrate intake restricted. Physical examination: Negative except for slight atrophy of left arm from attack of poliomyelitis he had in childhood. Laboratory examination: Blood, urine and Wassermann, negative. Achlorhydria. Dextrose tolerance test: Fasting, 0.066; 1 hour, 0.120; 2 hours, 0.085; 3 hours, 0.070; 4 hours, 0.060; 5 hours, 0.060; 6 hours, 0.060.

COMMENT: This patient, like many other cases of mild hyperinsulinism that we have had, came for treatment of "stomach trouble". Because of the abdominal discomfort relieved by taking food, a duodenal ulcer had been suspected by his physician. There were no X-ray evidences of ulcer. He had an achlorhydria, and no occult blood in his feces. Therefore, a diagnosis of ulcer can be ruled out. A low fasting blood sugar and low sugar readings, 0.060 per cent, four, five and six hours after the ingestion of dextrose at about the hours when he has symptoms and the fact that there are no evidences of disorders of the liver, pituitary, thyroid, and adrenals, make the diagnosis of hyperinsulinism positive. He was given dilute hydrochloric acid and placed on a hyperinsulinism diet including cream and fruits on arising, between meals, and at bedtime. His symptoms were relieved on this treatment.

Tachycardia and Hyperinsulinism. Case 4. Mrs. E. H. A. Birmingham, Ala. Housewife. Age 40. Height 5 feet 7 inches. Weight 125 pounds. First seen September 16, 1933, complaining of tachycardia, pains and soreness in upper part of abdomen—worse after getting tired. Feels better when she does not eat. A fasting sugar of 0.100 per cent seemed to indicate that this patient's tachycardia was not due to hyperinsulinism, but she was requested to return when she was having an attack of tachycardia. On February 22, 1934, the patient came in at 6:00 p. m. complaining of tachycardia, pain under heart and left shoulder and arm. Could not breathe well; was nervous and trembled all over. "Gas on stomach and intestines." She ate a few bites at 2:30—none since—pulse rate 200. Blood sugar, 0.056 per cent. She was given 50 grams of glucose and in a few minutes felt better, but pulse still 156. In 30 minutes patient felt much better; pulse was slower and blood sugar was 0.084. A few minutes later in her automobile on her way home the attack subsided and her pulse returned to normal. The attacks ordinarily lasted 9 to 10 hours, but this attack was cut short in an hour by the administration of dextrose solution. Glucose tolerance test March 21, 1934. Fasting, 0.080; 1 hour, 0.160; 2 hours, 0.120; 3 hours, 0.100; 4 hours, 0.066; 5 hours, 0.060; 6 hours, 0.060. When her blood sugar reached 0.066, she became very weak; pulse rate was 100.

Treatment: The patient was placed on a moderately low carbohydrate, high fat diet with frequent feedings and had no more attacks until she recently had an operation for removal of uterine fibroids. She had two attacks of techycardia following the operation, but made a good convalescence.

COMMENT: Waters[4] first reported a case of tachycardia associated with hypoglycemia. The blood sugar readings in his case were as follows: during seizures, 0.060 per cent; when fasting, 0.066 per cent. It will be noted that this patient did not complain of hunger,

but on the contrary said that she felt better when she did not eat. Wilder[15] pointed out that patients with hyperinsulinism sometimes have an actual distaste for food, even though eating will relieve their symptoms. It will also be noted that this patient's fasting blood sugar was normal, 0.100 and 0.080 per cent; but during an attack, the blood sugar was 0.056 per cent, and the ingestion of 50 grams of dextrose (corn sugar) in water relieved the paroxysm of tachycardia in less than an hour. Her glucose tolerance curve was distinctly hypoglycemic. In suspected hyperinsulinism one or more normal fasting blood sugar readings do not rule out hypoglycemia as a cause of symptoms. Blood sugars should be taken during the attacks, and glucose tolerance tests carried out for six hours may reveal hypoglycemia at the fifth or sixth hours when not infrequently the symptoms of which the patient suffers are reproduced. Recently we have had a case of paroxysmal tachycardia in which blood sugars during an attack and glucose tolerance tests were normal. Certainly, hyperinsulinism is not the only cause of paryoxysmal tachycardia, though it seems to be a factor in some cases.

Hysteria Due to Hyperinsulinism. Case 5. Mrs. I. S. Lineville, Ala. Housekeeper. Age 56. Height 5 feet 9½ inches. Weight 131¼ pounds. Symptoms: Complaining of "spells", mental lapses coming on suddenly. "Sees lights blinking and head runs away." Gets weak when she is hungry; has feeling of numbness, tachycardia, perspires and "shakes all over like a leaf". Always eructates freely during an attack and thinks that "gas pressing on her heart" is the cause of her "spells". Is afraid that she will die in attack. Attacks usually come on about 8 or 9 a. m., two or three hours after breakfast and last from 15 to 40 minutes. Is hungry all the time, but food doesn't seem to agree. Has insomia and gets up several times at night to eat—then gets back to sleep. Dextrose tolerance test November 7, 1933. Fasting, 0.080; 1 hour, 0.133; 2 hours, 0.100; 3 hours, 0.080; 4 hours, 0.050.

When her blood sugar reached 50 milligrams, the patient had a "spell"—began with tingling sensation in feet and hands, then numbness over body. Was very pale, nervous, weak and dizzy. Profuse perspiration and shook all over—complained of "trembling inside". She was given a glass of malted milk and in a few minutes was relieved. Treatment: Very great improvement by rest and diet.

COMMENT: This patient had been treated by several physicians who told her that there was "nothing the matter with her except that she had hysterics". Perhaps the basis for hysteria in many cases is hypoglycemia due to hyperinsulinism.

Hyperinsulinism and Neuro-Circulatory Asthenia. Case 6. Mrs. H. A. M. Macon, Miss. Age 54. Height 5 feet 3 inches. Weight 105 pounds. Symptoms: Nervousness, extreme weakness and trembling between meals. Is prostrated unless she eats every 2 or 3 hours. Nervousness and weakness exaggerated in an hour or two after eating sweets. Symptoms were reproduced during glucose tolerance test when blood sugar fell to 0.048 per cent, and were relieved immedintely by eating. Glucose tolerance test November 7, 1932. Fasting, 0.080; 1 hour, 0.100; 2 hours, 0.070; 3 hours, 0.060; 4 hours, 0.050; 5 hours, 0.048.

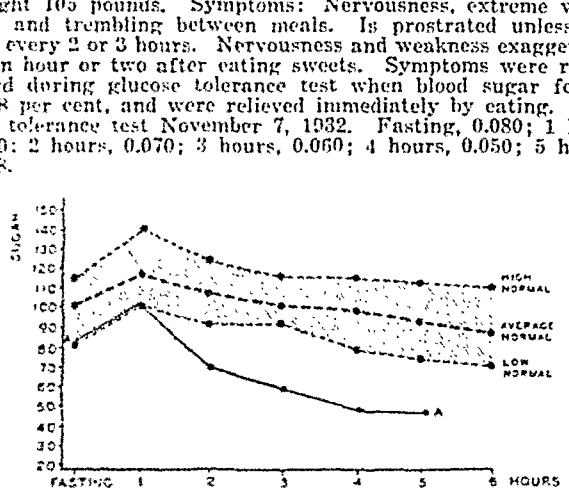


Chart 2. Case 6. A. Note low normal fasting blood sugar. The low readings two hours after ingestion of 75 grams of dextrose correspond to the time her symptoms occur.

Treatment: Rest, low carbohydrate, high fat diet, with frequent feedings relieved symptoms. Improvement has continued for two years.

COMMENT: This patient, a lovely woman, who was ambitious and wanted to work, would become exhausted from the slightest physical exertion and was almost an invalid because of hyperinsulinism. When food was given frequently, sufficient to maintain her blood sugar above the point at which hypoglycemic symptoms occurred, she was happy and efficient. This is the type of woman of whom it is said: "She has more energy than she has physical strength and endurance." Hyperinsulinism is one of the causes of fatigability and nervousness.

REPORTS OF CASES OF SEVERE HYPERINSULINISM

Psychotic Symptoms from Hyperinsulinism Following Undirected Reduction Diet. Case 7. Mrs. A. E. W. Birmingham, Ala. Housewife. Age 43. Height 5 feet ¾ inches. Weight 131 pounds. Symptoms: Duration 1 year, during which time she had reduced from 210 to 133 pounds. Two or three hours after meals and during the night, she had "spells" of weakness, nervousness, mental lapses and irritability. Mentally depressed and had ideas, or delusions, of persecution. The question of sending her to a psychopathic hospital was considered. Glycosuria was present at times. Pains in upper right quadrant suggested gall bladder disease.

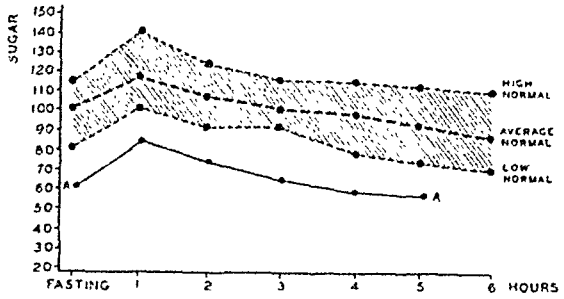


Chart 3. Case 7. A. Note the flat blood sugar curve. The peak of 0.080 per cent occurred one hour after the ingestion of 100 grams of dextrose. When her blood sugar fell to 0.060 per cent, the symptoms were reproduced, and she became so weak she had to lie down.

Treatment: Low carbohydrate, low caloric diet, consisting largely of 3 and 5 per cent vegetables and fruits, meat once a day, limited fats, with orange and tomato juice every 1 to 2 hours between meals and when awake at night. Patient has been on this diet for 2 years and is now in excellent health. The psychopathic symptoms have entirely subsided. This case illustrates the dangers from attempts at reducing without medical direction.

COMMENT: The blood sugar readings were quite low and the hypoglycemic symptoms pronounced. The results show the advisability of trying dietary management before resorting to surgery of the pancreas in even severe cases of hyperinsulinism. This case is a good demonstration of the effect of hypoglycemia on the mind. Powell[16] of West Monroe, Louisiana, in a general practice, has reported 15 cases of hyperinsulinism in which there are nervous and mental manifestations, all of whom were improved or completely relieved by giving them diets that maintained their blood sugars high enough to nourish the brain properly. Powell points out that the brain receives its nourishments from glucose circulating in the blood and that the brain has not the power to store up glycogen as have the muscles. Therefore when the amount of sugar in the circulating blood falls to below normal (hypoglycemia), the mind cannot function properly and nervous and mental symptoms result.

Abdominal Pain, Attacks of Unconsciousness and Delirium from Hyperinsulinism. Case 8. F. McC. Red Bay, Ala. Formerly druggist, now farmer. Age 30. Height 5 feet 9 inches. Weight 167 pounds. Symptoms: Recurring attack of intense headaches, agonizing abdominal pain, unconsciousness, with violent delirium. Is hungry all the time and feels weak when stomach is empty. Formerly drank 15 to 20 glasses coca-cola for relief but attacks grew worse. Appendix removed on account of abdominal pain but did not stop attacks. He was referred to us with a diagnosis of probable gall stones. Physical examination entirely negative except a low blood pressure, i. e., systolic 94, diastolic 65.

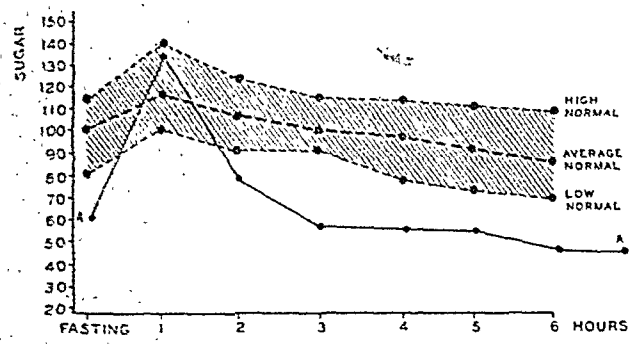


Chart 4. Case 8. A. Glucose tolerance curve is typical of hyperinsulinism. Note—Fasting blood sugar of 0.060 per cent and at 5 and 6 hours blood sugar levels at 0.050 per cent.

Treatment: On a low carbohydrate, high fat diet, with frequent feedings, this patient has had no attacks of unconsciousness or delirium and has had no abdominal pain in two years.

COMMENT: This case was referred to me with a diagnosis of probable gall stones, because of the intense abdominal pain, requiring on several occasions three-quarters grain of morphine for relief. Why there is abdominal pain in some of the severe cases of hyperinsulinism has not been proved; but in a number of such cases pain has been pronounced, and relieved in some by dieting and in others by removal of adenomas, or by partial resection of the pancreas. The excessive use of sweet soft drinks by overstimulation of the islands of Langerhans seems to have been a factor in producing hyperinsulinism. Certainly the taboo of soft drinks was a factor in relieving the symptoms. The low blood pressure, hypoadrenalism, was possibly due to exhaustion of adrenal function from the excessive use of caffeine contained in a soft drink of which the patient had been taking 15 or 20 glasses a day.

DYSINSULINISM

The uncontrolled secretion of insulin, excessive at times and resulting in hypoglycemia, which may alternate with or be followed by hypofunction of the islet cells with hyperglycemia, is manifested by inconstant symptoms of both hyperinsulinism and diabetes mellitus (hypoinsulinism). In some cases the hypoglycemic symptoms predominate and in others hyperglycemic phenomena are more pronounced. The symptoms of dysinsulinism may be mild and irregular, moderately severe and *bizarre*, or so severe that attacks of unconsciousness, convulsions, hypoglycemic coma and death may occur in patients known to have diabetes.

Symptoms of dysinsulinism may be brought out in dieting diabetic patients, particularly in the mild overweight cases; but severe diabetes may co-exist with severe hyperinsulinism. In such cases the hypoglycemic symptoms usually present the more serious problem.

My first case diagnosed as dysinsulinism was in January, 1924,[1] An obese woman, who a year before when she weighed 210 pounds (95 Kg.) had had glycosuria, was sent to me as a diabetic patient. She had reduced, by dieting, to 160 pounds, (72.6 Kg.) and complained of having "spells of weakness and nervousness" at about 1 or 2 o'clock in the morning. She had found from experience that eating would relieve the symptoms, so that she kept an orange or a glass of milk on the table by her bed. Her blood sugar during an attack was 0.047 per cent. She was relieved promptly by frequent feedings of a low carbohydrate diet, consisting largely of the 5 and 10 per cent vegetables and fruits, with sufficient proteins and fats. Since then I have had three other cases of dysinsulinism.

CASE REPORTS OF DYSINSULINISM

Mild Diabetes and Hypoglycemic Symptoms. Case 9. C. H. M. Corinth, Miss. Laundry manager. Age 41. Height 5 feet 5 inches. Weight 127 pounds. Symptoms: Polyuria, glycosuria, nervous, weak feeling in mid-morning and afternoon relieved by taking food. Duration 3 weeks. Fasting blood sugar 0.060 per cent. Glycosuria constantly for 2 years. Four grams of sugar excreted in 24 hours. Glucose tolerance test November 17, 1930. Fasting, 0.060; ½ hour, 0.100; 1 hour, 0.166; 2 hours, 0.133; 3 hours, 0.100; 4 hours, 0.083; 5 hours, 0.058.

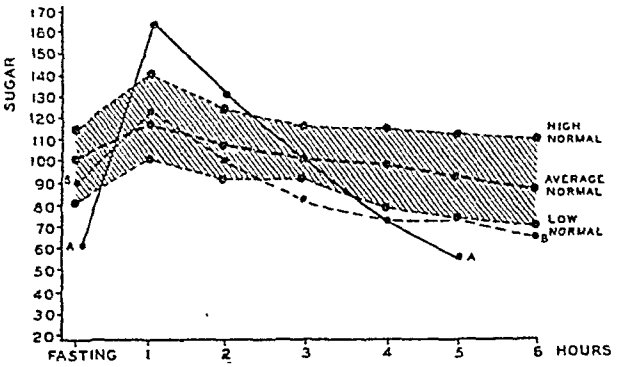


Chart 5. Case 9. A. Note low fasting blood sugar, high peak and low reading at end of 5 hours. His hypoglycemic symptoms synchronized with the low sugar readings.

B. Practically normal blood sugar curve after 4 years of dieting.

Treatment: Hypoglycemic symptoms relieved on weighed and measured diet of 120 carbohydrate, 60 protein and 180 fat with food every 2 hours but glycosuria persists. Has increased 12 pounds in weight.

COMMENT: Four years ago this patient had the blood surgar curve of a mild diabetic, but note that the fasting blood sugar was 0.060 and 5 hours after the ingestion of 100 grams dextrose, his blood sugar had fallen to 0.058 per cent. He had hypoglycemic symptoms before meals. Since he had sugar in his urine at all times, even when he was having hypoglycemic symptoms, with blood sugar levels of 0.060 and 0.058 per cent, no doubt due to hyperinsulinism, it appears that the pancreas may have something to do with the "low renal threshold". After rigid dieting for four years, this patient has a normal blood sugar curve. In other words, his carbohydrate tolerance seems to be normal, yet he has sugar in his urine constantly.

Subacute Pancreatitis and Dysinsulinism. Potential Diabetic. Case 10. June 1, 1932. Mrs. L. E. V. Birmingham, Ala. Housewife. Age 29. Height 5 feet 4 inches. Weight 132 pounds. Symptoms: Duration 2 months; confined to bed 3 weeks. Miscarriage followed by pelvic infection 6 months ago. For past 2 months had had fever, pain and tenderness in upper part of abdomen. Nausea and vomiting at times. "Smothering spells" when heart beats very fast. Is very nervous and weak. Pulse rate on examination was 108. Fasting blood sugar was 0.062 per cent when she was given 100 grams of dextrose for glucose tolerance test. In a few minutes her pulse was 72, and she was quite comfortable.

	Fasting	1 hr.	2 hrs.	3 hrs.	4 hrs.	5 hrs.
Blood sugar	0.062	0.133	0.200	0.133	0.120	0.090
Urine sugar	0	0	4V	4V	4V	4V

Treatment and Result: Has improved very much on low carbohydrate, high fat diet with frequent feedings of orange juice or tomato juice between meals; but has increased 12

pounds in weight. No sugar in urine since the glucose tolerance test. Her fasting blood sugar two weeks after treatment 0.100 and one month after treatment 0.080 per cent.

COMMENT: The pelvic infection apparently was the cause of the pancreatitis with disturbed carbohydrate metabolism. This patient is regarded as a potential diabetic.

Dysinsulinism Associated with Recurring Attacks of Pain and Tenderness over Pancreas, Nausea and Vomiting. Relieved by Resection of the Pancreas. Potential Diabetic. Case 11. Mrs. J. H. C. Hanceville, Ala. Age 32. Height 5 feet 7 inches. Weight 115 pounds. Symptoms: Referred by Dr. Earle Drennen for recurring attacks of abdominal pain, nausea, vomiting, "spells" of weakness and fainting before breakfast, and when stomach was empty; relieved by taking food. Exploratory laparotomy June, 1932, revealed no pathology, but the appendix was removed. Patient obtained no relief from the operation. Marked tenderness and soreness in the upper left quadrant and the attacks of weakness continued.

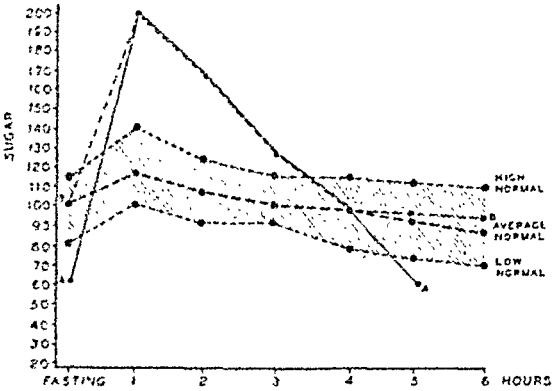


Chart 6. Case 11. A. Dysinsulinism glucose tolerance curve before operation.

B. Glucose tolerance curve 2 months after operation. There is still the high (diabetic) level; but normal levels fasting and 4, 5 and 6 hours after the ingestion of 100 grams of dextrose.

Treatment: Dietary management over a period of five months failed to give relief. An operation was performed by Dr. Earle Drennen on March 27, 1934. The pancreas appeared normal but on account of the pain and hypoglycemic symptoms about half the body and all the tail of the pancreas were resected. The patient made a good operative recovery and has had no attacks of abdominal pain or hypoglycemia since the operation.

COMMENT: The blood sugar curve in this case alternates hypoglycemic with hyperglycemic phases, i. e., a low fasting blood sugar, 0.060 per cent. A sudden drop from 0.100 to 0.050 per cent in from the fourth to fifth hours, and a diabetic curve from one to four hours after taking the dextrose. The patient was an invalid from recurring attacks of abdominal pain, nausea and vomiting in addition to her hypoglycemic symptoms, i. e., marked weakness, fainting spells, etc. Blood sugar studies revealed disturbed carbohydrate metabolism evidently of pancreatic origin. An exploration and resection of the pancreas was clearly indicated and the relief of symptoms from the operation seem to have justified the procedure. In other words, the resection of the pancreas removed the hypoglycemic phase, but did not affect the diabetes. The latter is controlled by dieting.

HYPERINSULINISM AND CONVULSIVE SEIZURES

In discussing the relationship of hyperinsulinism to epileptiform attacks, I desire it distinctly understood that I do not believe that hyperinsulinism is the cause of epilepsy.[19] Nor do I think it is the sole etiological factor in any case of epilepsy. I believe, however, that in a patient with the epileptic *anlage*, or predisposition, the hypoglycemia resulting from hyperinsulinism may be a precipitating factor—"the trigger"—in producing convulsive seizures.[20]

In the light of recent investigations it seems probable that in some cases the periodic attacks of convulsions and unconsciousness in epileptic patients may be manifestations of the hypoglycemia resulting from the spontaneous excessive secretion of insulin by the islet cells of the pancreas (hyperinsulinism). A number of cases reported by careful and capable clinicians, in which the diagnosis of epilepsy had been made, have been associated with hypoglycemia assumed to be due to hyperinsulinism; and in some of these cases the convulsions have been controlled by dieting. In other cases of periodic epileptiform convulsions associated with hypoglycemia, adenomas of the pancreas have been found at operation, and their surgical removal has resulted in clinical cures of patients who otherwise would have been doomed to live only a few months, or a few years, with the constant fear of epileptiform seizures hanging over them.

If the hypoglycemia due to hyperinsulinism is proved to be a factor in the periodic attacks of convulsions in some of the cases now classified as idiopathic epilepsy, then with the application of our present knowledge of the dietary management of hyperinsulinism it seems probable that this type of epilepsy, unless associated with neoplasms of the pancreas, may be controlled by a diet that will maintain the patient's blood sugar level at a point high enough to prevent the seizures. The fact that a number of persons who had periodic attacks of convulsions, some of which were thought to have been epileptic seizures until hyperinsulinism was diagnosed, have been cured by the removal of adenomas involving the islet cells of the pancreas, should bring hope to the patient who has periodic attacks of convulsions associated with hypoglycemia of pancreatic origin which cannot be controlled by dieting.

REPORTED CASES OF PATIENTS AFFECTED WITH EPILEPTIFORM ATTACKS

A number of cases of recurring attacks of convulsions and unconsciousness were reported by other clinicians before we observed our first case of epilepsy in a patient who had hypoglycemia apparently due to hyperinsulinism, and a number of other cases have been reported since then. The first pathologically proved case of hyperinsulinism and the first case reported in which attacks of convulsions were proved to be due to spontaneous hypoglycemia (blood sugar, 0.030 per cent) was reported by Wilder, Allen, Powers and Robertson[21] in 1927. Thalheimer and Murphy[22] in 1928 reported a death from hypoglycemic convulsions and coma (blood sugar, 0.033 per cent). As in Wilder's case the autopsy showed a primary carcinoma of the islands of Langerhans.

Neilson and Eggleston[16] in 1930 reported three cases of functional dysinsulinism seizures (blood sugars, 0.050, 0.069 and 0.064, respectively,) in which the epileptiform attacks were controlled by dieting. Weil's[15] remarkable case of "functional dysinsulinism" with epileptiform convulsions in which the blood sugar level fell to zero, was relieved by dieting. She has had one convulsion in three years, and her fasting blood sugar levels now are normal (0.082 per cent).

The first case of hyperinsulinism in which the diagnosis of a probable neoplasm of the pancreas was made from blood sugar studies (0.040 per cent), and the patient clinically cured by surgical removal of a small primary carcinoma of the islands of Langerhans, was reported by Howland, Campbell, Maltby and Robin-

son[23] in 1929. Five cases of successful surgical removal of islet cell adenomas from the pancreas have been reported by Washington University surgeons. In all five cases the attacks of convulsions and unconsciousness were cured clinically by the operation (Carr[24] et al, Graham,[25] Womack,[26] Smith and Seibel[27]). Best, Schmidt and Sevringhaus[28] reported the successful removal of a carcinoma of the islands of Langerhans for *status epilepticus*, due to hypoglycemia. A number of other cases of the removal of adenomas for the relief of hyperinsulinism have been reported.

The first partial resection of the pancreas for the relief of hyperinsulinism was by Finney[29] in 1928. Judd[30] has resected the pancreas for hyperinsulinism in eight cases. A case of narcolepsy reported by Seale Harris[20] was operated upon by Adrian Taylor, who resected about half the body and all of the tail of the pancreas. The patient has had no attacks of unconsciousness since the operation two years ago. More recently three resections of the pancreas for hyperinsulinism have been performed by Evarts Graham and Womack,[31] in one of which, an infant fifteen months old, reported by McKim Marriott,[32] the convulsions and other hypoglycemic symptoms were relieved by a subtotal resection (seven-eighths) of the pancreas.

Space will not allow even the mention of all of the approximately thirty successful operations on the pancreas for hyperinsulinism that have been reported. The clinical cures of these patients having recurring attacks of convulsions and unconsciousness are a triumph of American surgery, because without operations they would have been doomed to miserable lives and early deaths from the hypoglycemia, due to hyperinsulinism.

Epilepsy Following Abdominal Injury. Case 12. October 3, 1932. Mrs. E. R. V. Birmingham, Ala. Housewife. Age 28. Height 5 feet 4½ inches. Weight 93 pounds. Symptoms: Paroxysms of convulsions and unconsciousness at varying intervals for 11 years. First attack occurred about one month after abdominal injury from which she was in bed for three weeks. Attacks occur now only during menstruation. Is weak and nervous for an hour before meals. Feels better after eating.

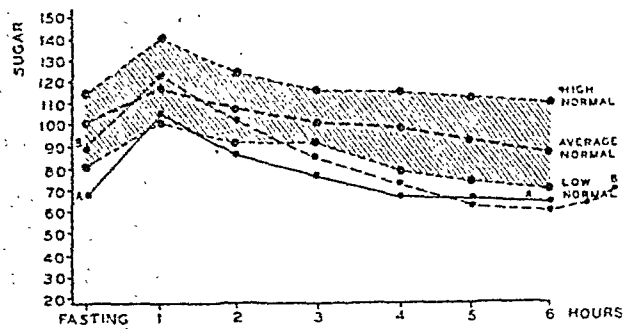


Chart 7. Case 12. A. Blood sugar readings and glucose tolerance test between menstruation.
B. Glucose tolerance curve during menstruation.
Note—when patient's blood sugar fell to 0.050 she had a light but typical epileptic convulsion. She was then given one and one-half grains of luminal. In one hour her blood sugar had risen to 0.068 per cent.

Treatment: On a low carbohydrate, high fat diet with orange and tomato juice between meals this patient passed through several menstrual periods without convulsions. Recently she has discontinued dieting, and the convulsions have recurred at some of her menstrual periods.

COMMENT: The evidence is strong in this case that trauma of the pancreas was the exciting cause of the epilepsy. Since this patient had a *grand mal* attack when her blood sugar fell to 0.050 per cent, it seems that hyperinsulinism is the exciting cause of the convulsions. Since this patient will not carry out her diet, a partial resection of the pancreas seems indicated and justifiable.

Narcolepsy and Hyperinsulinism. Clinical Cure by Partial Resection of Pancreas. Case 13. July 1, 1932. E. K. Parrish, Ala. Farmer, formerly miner. Age 20. Height 5 feet 9 inches. Weight 142 pounds. Symptoms: Recurring attacks of unconsciousness. Abdominal pains, not related to eating. Tenderness over the pancreas. Operation for appendicitis was performed without relief. Became hungry and weak an hour or two after eating. Food gave relief. Fasting blood sugar 0.050 per cent. On account of the abdominal pains, not relieved by an appendectomy, a diagnosis of "duodenal ulcer or gall bladder disease" was made by the patient's family physician.

Treatment: Patient was comfortable for 2 weeks in hospital on weighed and measured diet of 100 grams carbohydrate, 75 grams protein and 180 grams fat, with frequent feedings. Symptoms recurred after returning to home diet. Exploratory operation advised for removal of insuloma if present; if not resection of portion of pancreas. Operation by Dr. Adrian Taylor revealed pancreas normal in appearance; one-half body and tail were resected. Wound closed without drainage. Uneventful recovery. No pain and no symptoms of hypoglycemia in two years. Apparent clinical cure. Repeated fasting blood sugars at intervals of from one to three months for the past two years have been normal. A recent glucose tolerance test was normal.

COMMENT: An exploratory operation in this case would have been justifiable on account of the abdominal pain and tenderness; though the hypoglycemic symptoms were most pronounced. Relief of the symptoms, with normal blood sugar readings, not to mention the improved mentality and changed personality of the patient, for a period of two years seems to place the operation of partial resection of the pancreas for severe hyperinsulinism without adenomas on the same basis as a partial resection of the thyroid for hyperthyroidism, without adenomas.

Hyperinsulinism, Chronic Pancreatitis, Appendicitis and Epilepsy: Appendectomy and Partial Resection of Pancreas. Case 14. December 21, 1931. C. H. Durham, N. C. Teacher. Age 27. Height 5 feet 9 inches. Weight 181 pounds. Symptoms: Three typical epileptic convulsions in four months. Attacks occurred several hours after meals; bit his tongue in each attack. Severe burn on foot from an open grate in one attack. Has had petit mal attacks for eight years or longer.

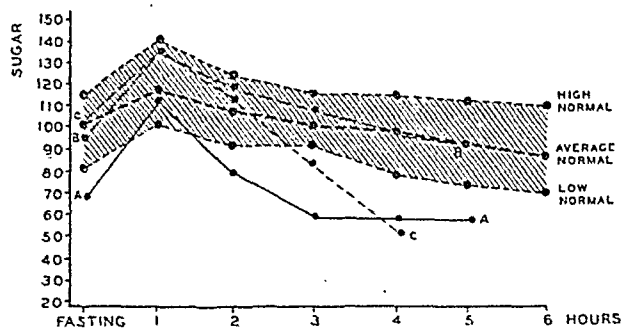


Chart 8. Case 14. A. Blood sugar curve in glucose tolerance test December, 1931.
B. Blood sugar curve in glucose tolerance test June 5, 1934.
C. Blood sugar curve in glucose tolerance test June 19, 1934.

One blood sugar curve, B, was about normal, while the other two, A and C, showed hypoglycemia, proving that one glucose tolerance test is not sufficient to establish, or rule out, a diagnosis of hyperinsulinism anymore than that one basal metabolism test may not give sufficient evidence on which to make a diagnosis of hyperthyroidism.

Treatment: Low carbohydrate, normal protein and fat diet, with orange or tomato juice one, two and three hours before meals. No medicines. Improved for a year; the seizures were fewer and less severe. For the past year he has not adhered to diet and attacks more severe and more frequent.

COMMENT: This patient, a highly educated teacher, lost his position on account of epilepsy, and his future seemed hopeless. Since hypoglycemia may have been

a precipitating cause of his *grand mal* attacks and since other patients have been relieved of similar attacks by removal of an adenoma, or partial resection of the pancreas, an operation was advised. Dr. Earle Drennen operated June 20, 1934. About one-half the body and all the tail were resected. Microscopic section of the pancreas showed marked pancreatitis. While the patient is convalescing, the ultimate results from the operation cannot be predicted. The fact that he had a chronic pancreatitis indicates that his pancreas was the essential factor in the hypoglycemia and that the case is one of true hyperinsulinism.

Pituitary Epilepsy and Hyperinsulinism. Case 15. K. I. Birmingham, Ala. Age 17. Height 5 feet 10 inches. Weight 219 pounds. He weighed 238 pounds at the age of 16. Brief mental lapses were of almost daily occurrence. He was sleepy after attacks. He had had six grand mal attacks in the last four months. He had a voracious appetite and ate excessively of sweets. The family history was negative. He was of normal size at birth, but became very much underweight from repeated illnesses including colitis, acidosis, influenza, otitis media, and so on. He did not walk until he was 2½ years of age. He had convulsions once at the age of four years. Soon afterwards he began having attacks of mental lapses when he became frighted from seeing "little men". At about five years of age he began to grow, and at 10 years of age had an enormous appetite. He craved sweets. At 13 he weighed 175 pounds and at 16, 238 pounds. He has large shoulders and hips, long arms, large hands and feet; and is very powerful physically. The primary diagnosis was dyspituitarism in the hypopituitary phase. The secondary diagnosis was hyperinsulinism. Glucose tolerance test at the beginning of treatment showing fasting sugar 0.066; 1 hour, 0.120; 2 hours, 0.100; 3 hours, 0.066⅔; 4 hours, 0.066; 5 hours, 0.066; 6 hours, 0.066. The glucose tolerance test six weeks later, after taking pituitary tablets, was fasting, 0.100; 1 hour, 0.154; 2 hours, 0.120; 3 hours, 0.100; 4 hours, 0.080; 5 hours, 0.066; 6 hours, 0.080.

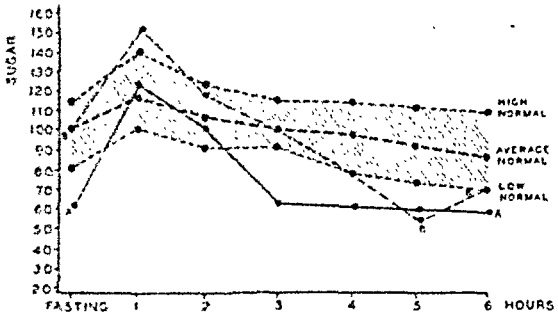


Chart 9. Case 15. A. Glucose tolerance curve. B. Tolerance curve showing effect of 42 grains of pituitary extract a day.

Treatment consisted of a hyperinsulinism reducing diet and 42 grains pituitary extract a day. His mentality is improved. He has reduced to 193 pounds. He had had no attacks of mental lapses and no *grand mal* attacks in two months, whereas, before he began the use of the pituitary tablets combined with a hyperinsulinism reducing diet, he had two or three daily periods of brief mental lapses and three convulsions the week before the treatment was begun. Two or three months later this patient had 2 or 3 epileptic attacks, whereupon his parents became discouraged, discontinued the treatment and gave him a patent epileptic cure—no doubt containing large doses of the bromides. They report that he has had no convulsions in several months.

COMMENT: A case of epileptiform convulsions associated with hypopituitarism and hyperinsulinism is reported to illustrate the relation of the hypophysis to insulin secretion. The primary diagnosis was dyspituitarism. No doubt the stage associated with the rapid growth and increase in weight was due to the excessive secretion of the pituitary hormone, and ended about the period of adolescence when the hypopituitary stage came on. The islands of Langerhans without the regulating effect of the antagonistic pituitary hormone began to secrete an excess of insulin (hyperinsulinism), and hypoglycemia and *petit mal* and *grand mal* attacks followed.

SUMMARY AND CONCLUSIONS

1. Fifteen cases are reported illustrating clinical types of hyperinsulinism.

2. The varied manifestations of hypoglycemia, due to the excessive secretion of insulin, seem to indicate that hyperinsulinism may be responsible in some cases for symptoms that simulate, or are associated with, many disorders, particularly those classified as neuroses of various organs.

3. Cases of hyperinsulinism associated with recurring attacks of unconsciousness and convulsions, including cases of actual epilepsy, are reported.

4. One case is reported of an actual psychosis found associated with hyperinsulinism and in which there has been relief of symptoms for two years by dietary management.

5. Attention is called to Powell's study of fifteen cases of hyperinsulinism. Powell's conclusions[17] present a viewpoint that should be considered by the medical profession: "Ample case reports are in the literature to show that this condition (hyperinsulinism) causes symptoms varying from drowsiness to narcolepsy, from vertigo to epilepsy, from mental deficiency to mental degeneration. Unfortunately all the cases are not in the literature—they are to be found in every doctor's clintele and, sad to relate, are most probably untreated.

"A careful study of the food supply of the brain should be made in all nervous and mental cases. This may be accurately determined by a study of the blood sugar concentration."

6. Routine fasting blood sugars and blood sugar studies during "spells", as the patients usually call hypoglycemic attacks, may reveal the cause of various neuroses that can be prevented and controlled by dieting.[32]

7. Glucose tolerance tests should be carried out for six full hours. The glucose tolerance test of three or four hours as carried out in diabetes is usually of little value in making a diagnosis of hyperinsulinism.[34]

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DIABETIC COMA IN CHILDREN

By

HENRY J. JOHN

CLEVELAND, OHIO

DIABETIC coma in children no longer presents the same problem which it did even ten years ago. The outcome in diabetic coma depends on two things: (1) how early the treatment is started, and (2) how adequate it is. There is no standard dose of insulin in such an emergency. The amount of insulin necessary to bring a child out of coma varies considerably, as is shown in Figures 1 to 12.

Heimann-Trosien and Hirsch-Kaufmann[1] called attention to the fact that the younger the infant the more carefully must one adjust the insulin dosage. Lauritzen[2] and Simon,[3] who treated two children, aged two and three-fourths years and four years, respectively, succeeded in their prompt recovery from coma on small dosages of insulin. Arndt and Welcker[4] treated an infant three months old in coma who died ten hours later after but four units of insulin. The child became edematous, which fact the authors interpreted as a hypoglycemic reaction. I would rather suspect that the death resulted not from the four units of insulin but rather from insufficient dosage of insulin. This patient was treated in the early period of insulin therapy at a time when physicians were more or less afraid of the preparation.

Boyd[5] emphasized the importance of early treatment of diabetic coma and her statistics are quite convincing. At the Hospital for Sick Children at Toronto, where fifty-one coma cases in children were treated up to that time, she summarized the results as follows:

The Effect of Delay in Treating Diabetic Coma on Its Mortality
(Boyd)

Time Hours	Number Cases	Number Deaths	Percentage Mortality
0-24	15	0	0
24-48	10	2 (d. pneum.)	20
48-96	17	8	41
5 days or longer	9	7	77

Submitted August 9, 1934.

Boyd[6] also reported ninety-five cases of diabetes mellitus in children under fifteen years of age of whom 37 or 38 per cent had coma.

In my series of 218 children (first and second decade) coma occurred in fifty instances or 23 per cent over a period of thirteen years. These may be divided into two groups: (1) those that were under my immediate care during coma (early or late), and (2) those who were cared for by the family physician during the coma. The data in these two groups are striking and instructive and are presented in Tables 1 and 2. In

TABLE I

Data on Diabetic Children in Coma of Group of 218 Under Author's Care

	No.	Age Years	Year	Living	Dead	Blood Sugar	Plasma Acetone	Plasma CO_2	Lipemia
Girls	1.	1.5	1925	+		310	+	32.6	
	2.	2.5	1926	+		428			
	3.	3.	1926	+		485	+ + +		
	4.	3.	1926	+		375			
	5.	5.	1929	+		256*	+ + +	25.2*	
	6.	7.	1932	+		564	+ + +	18.5	
	7.	9.	1929	+		552*	+ + +	29. *	
	8.	10.	1926	+		666	+ + +		+
	9.	11.	1922		+	300		25.2	
	10.	12.	1934	+		270*	+ + +	21. *	
	11.	15.	1922	+		447	+ +	24.	+ + +
	12.	15.7	1931		+	836	+	9.9	
	13.	18.	1927	+		410	+ + +	27.1	
	14.	20.	1924	+		405	+ + +		+ + +
	15.	22.	1926	+		626	+ + +	13.7	
Boys	16.	2.	1927	+		476	+ + +	13.7	
	17.	4.	1922	+		440	+ + +		+ + +
	18.	7.	1925	+		475	+ +	27.1	
	19.	8.	1926	+		460	+ + + +	15.7	
	20.	8.	1930	+		606	+ + +		
	21.	9.	1927	+		440	+ +	20.2	
	22.	13.	1920	+		688*	+ + +	13.2*	
	23.	14.	1929	+		405		21.4	
	24.	14.	1928	+		543*	+ + +	44.3*	
	25.	15.	1928	+		460*	+ + +	38.6*	
	26.	16.	1926	+		366	+ + +	23.3	+ + +
	27.	16.	1931		+	994	+ + +	9.9	
	28.	17.	1923		+	652	+ + +	17.6	
	29.	17.	1931	+		353	+ + +	11.8	
	30.	18.	1922		+	267	+ + +		
	31.	20.	1932	+		360*			

*After insulin.
Cases 9, 27, and 28 died in one hour after admission.
Cases 30—pre-insulin era.

Table 1, those under my immediate care, there is an equal division between the two sexes. This group comprises thirty-one cases and of these five died; one

in the pre-insulin era; three patients were moribund when they were brought to the hospital and died within one hour after their admission. Thus, if these four cases in which the mortality was unpreventable are eliminated there remains but one death, a mortality rate of 3.2 per cent.

TABLE II

Data on Diabetic Children in Coma of Author's Group of 218 Treated by the Family Doctor During Coma

	No.	Age Years	Year	Living	Dead	Blood Sugar	Remarks
Boys	1.	6.5	1928		+		At home
	2.	7.	1921		+		At home
	3.	9.	1924		+		At home
	4.	10.	1924		+		At home
	5.	11.	1922		+		At home
	6.	12.	1925		+		Quack victim
	7.	13.	1923		+		At home
	8.	14.	1928	+		720	Hospital
	9.	14.	1921		+		At home
	10.	14.	1927	—		444	Hospital
	11.	16.	1926		+		At home
	12.	18	1932		+		Appendectomy
Girls	13.	3.	1928	+			At home
	14.	3.5	1927		+		At home
	15.	14.	1924		+		Hospital
	16.	19.	1921		+		Hospital
	17.	19.	1932		+		At home
	18.	20.	1927		+		At home
	19.	20.	1932		+		At home

In Table 2 are tabulated the results of treatment of cases of coma by the family physician. These contrasting results are cited without malice but merely to stress the point that diabetic coma should be treated adequately. Of nineteen patients with coma, but three survived. My object in presenting this contrasting picture is to show the evolution of treatment with insulin in the first decade after its discovery. The family doctor during this first decade was afraid of insulin and either did not use it at all or else used it in such absurdly small doses that he failed to get results. We must look upon the first decade of the insulin era as a stage of transition and of increasing knowledge of how to use insulin. Probably no future decade will ever duplicate data such as these.

TABLE III

Data on a Series of Children in Coma Reported by Joslin[7]

Age Years	Year	Living	Dead	Blood Sugar	Diacetic Acid
13.5	1929	+		660	+ + + +
18.8	1929	+		290	+ + +
18.9	1929	+		320	+ + +
4.2	1924	+		420	+ + +
18.7	1928	+		260	+ + +
17.7	1924	+		720	+ + + +
10.5	1929	+		440	+ + +
11.9	1929	+		410	+ + +
15.7	1929	+		250	+
14.0	1929	+		620	+ +
3.6	1929	+		260	—
12.2	1929	+		540	+ + +
13.3	1929	+		930	+ + +
19.9	1930	+		280	+ + + +
9.9	1930	+		350	+ + + +
13.1	1930	+		350	+ +
14.5	1930	+		500*	0
13.8	1930	+		230	+ +
17.2	1930	+		350	+ + +
6.9	1930	+		470	+ + + +
14.1	1930	+		320	+ +
13.2	1930	+		580	+ +
14.0	1931	+		420	+ + +
13.5	1931	+		660	+ +
15.4	1931	+		320	+ +
7.1	1931	+		340	+ + + +
14.7	1931	+		480	+ + + +
15.9	1931		+	460	+ + +
17.2	1931	+		300	+
12.8	1931	+		460	+ +
14.1	1931		+	580	+ + +
17.3	1931	+		330	+ +
18.4	1931	+		600	+ + +
16.9	1931	+		320	+ + + +

*After insulin.

In Table 3 are tabulated the results of treatment of coma in children by Joslin.[7] This table was compiled from his larger series of cases of coma (children and adults) published in 1929. I have simply collected all the juvenile cases from this group. In a total of thirty-four children (first and second decade) there were but two deaths between the years 1929 and 1931. This represents a mortality of but 5.8 per cent against a mortality of 17.2 per cent among the adults in this same series. One would hardly get the impression from this that there is more risk in handling coma in a child than in an adult, but that the reverse is actually true.

TABLE IV

Mortality from Coma in a Series of 218 Children (Author's Experience)

No.	Age at Death Years	Sex		Duration Diabetes Years
		Male	Female	
1.	6.5	+		1.
2.	7.	+		0.01
3.	9.	+		5.
4.	10.	+		1.
5.	11.	+		0.01
6.	12.	+		0.75
7.	13.	+		1.
8.	14.	+		0.01
9.	15.7	+		2.
10.	16.	+		3.
11.	18.	+		4.
12.	3.5		+	0.1
13.	14.		+	2
14.	16.		+	8.
15.	17.		+	0.01
16.	18.		+	0.5
17.	19.		+	0.25
18.	19.		+	1.
19.	20.		+	7.
20.	20.		+	5.

Dead in the first year of diabetes—12 or 57.1%
Dead in the second year of diabetes—2 or 9.5%
Dead above that period—7 or 33.3%

In Table 4 I have compiled all the deaths from the two groups according to age, sex and the length of diabetes. This shows that of the total mortality 57.1 per cent died during the first year of diabetes.

Prompt and adequate treatment in coma produces good results in a child and adult alike. I have prepared twelve charts on my series of cases to show graphically the main procedures and the laboratory data in each case. These charts show that there is a considerable variation among the different children.

As little as 61 units of insulin had been used to bring a patient out of coma and as much as 685 units were used in order to accomplish the same result. There are many factors which enter into this, including the duration of coma before the treatment was started, the severity of the diabetes, the duration of the diabetes, the rapidity of the onset of the coma, the presence or absence of intercurrent infection, the dosage of insulin before the onset of coma, whether or not the child is sensitive to insulin or is "insulin resistant", the condition of the child's liver. Various other factors also could be enumerated.

The charts represent a marked difference in response, due to the above factors. However, in the final analysis, the main point is: How early has the treatment been started and how adequately pursued? *Coma in a child represents a major medical emergency and as such requires radical treatment, as in a surgical emergency.* Hence, prompt hospitalization is necessary if the mortality rate is to be kept low. We must offer all we can to such a child in order to preserve life. Furthermore, it is not merely the saving of life but the preservation of function which is at stake. Prolonged coma increases the severity of diabetes. In treating a child with diabetic coma, one is always confronted with the problem of whether it will be possible to neutralize the damage promptly and get the child

out of coma with approximately the same insulogenic function which existed before the child went into coma or whether the child will emerge from this catastrophy with a markedly lessened insulogenic function.

Case 3893, Chart No. 11, presents an example of diminished insulogenic function after coma. His diabetes was very mild before his coma, and I was able to treat him without insulin by regulation of diet and he had a normal blood sugar morning, noon and night and sugar-free urine. He contracted an acute infection, measles. The family doctor in a small town naturally did not appreciate the significance of an infection in such a mild case of diabetes. He did nothing to protect the child during this infection with the result that the patient went into coma a few weeks later. The child no longer has mild diabetes, but is a severe diabetic for all time. That is the important point to bear in mind, that even a mild diabetic can become a severe one, if he is not protected during the course of an infection.

Case No. 2546 in Chart 4 represents a child who was in perfect health and did not know she had diabetes. An intestinal "flu" threw her into coma in twenty-four hours and that was when the diabetes was first discovered. With prompt treatment, she emerged from coma with mild diabetes and for months at a time she did not need insulin, but merely dietary treatment. Even though she was but mildly diabetic, a simple cold threw her into a second coma four years later. This child one day went into coma while away from home. The doctor who was summoned gave her immediately 40 units of insulin intravenously and an hour later was ready to give her 40 units more when I was consulted by telephone. Upon explaining to me the child's symptomatology, it was quite evident that she was not in diabetic coma but in insulin shock and I directed that she receive 10 c.c. of a 50 per cent glucose solution intravenously which brought the child to consciousness within ten minutes. Surely, were the safeguards in a young body limited to a narrow zone, this child would not be here today.

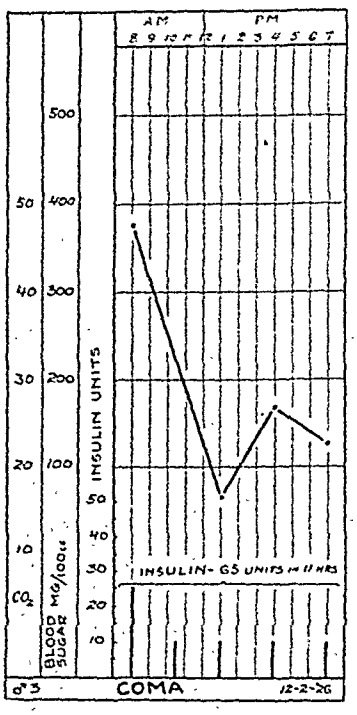


Chart 1. Case No. 650. A Jewish boy who developed diabetes in 1924. It followed shortly after a cold when he was two years old. There is no diabetes in the family. The onset of coma was in the second year of his diabetes. He had scarlet fever in September, a bad cold in November and went into coma on December 2. He responded promptly to insulin alone.

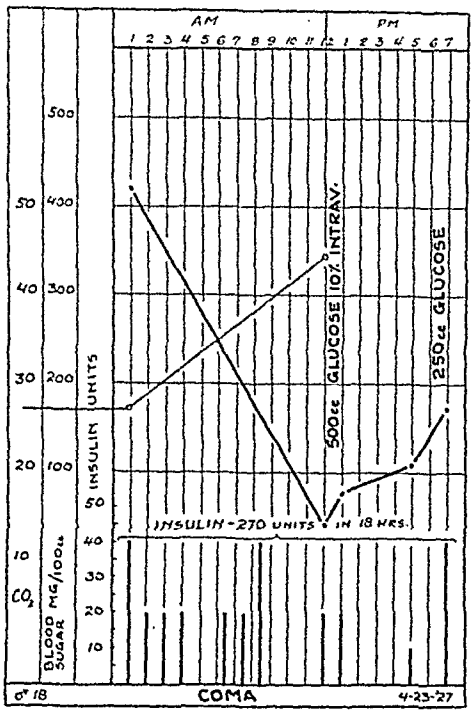


Chart 2. Case No. 1692. A Gentile boy 18 years of age whose diabetes began in April, 1927. This was preceded by lobar pneumonia and diabetes appeared a few days after that. When I first saw him he was in coma, April, 1927, with a blood sugar of 410 and CO_2 27.1 after two doses of insulin. In eighteen hours he was given 270 units of insulin together with intravenous glucose. The response was prompt but his insulin requirement was heavy for a whole month. Acidosis followed in six months, tubercucolis in 1928, jaundice in 1930 and he died of tuberculosis April 12, 1932.

In Chart 3, Case No. 1555, is that of an infant but two years of age. I started giving her only five units of insulin every half hour for several hours as I naturally was afraid to administer larger dosage to a child so young. This was later increased to 10 units every half hour until she came out of coma. But even in such a young child, 125 units were used within ten hours.

Case No. 2847, Chart 8, presents a boy 15 years of age, who had severe diabetes. In the first part of the chart, one sees that a heavy insulin dosage was necessary in order to control the acidosis. One would expect that if this boy ever went into coma, a large quantity of insulin would be required. The second half of the chart shows what happened one year later when he went into coma and 570 units of insulin were used without result.

It is for the above reasons that one can not treat a case of coma in childhood according to a formula. There is no formula which will fit all cases, but each case presents an individual problem which must be dealt with individually and a sufficient amount of insulin, glucose and saline must be given to bring about the desired result. Experience alone will dictate the procedure. Also, one must be ever on the alert for relapses. Sometimes a child emerges from coma only to relapse into coma a few hours later if the routine is discontinued. And it may be more difficult to bring him out of the relapse than it was to bring him out of the original coma. One must be on the alert until one is assured that all the danger is past. And when the coma is past, give the child enough insulin to control his metabolism so as to save as much function as possible.

SYMPTOMATOLOGY

The most common symptoms of acidosis which is the precursor of coma is the *gastric upset.* The children

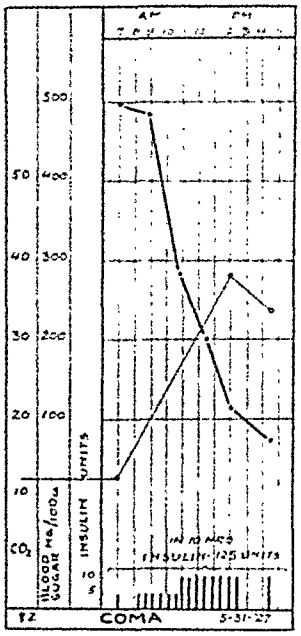


Chart 3. Case No. 1555. A Gentile girl who developed diabetes in 1927, at the age of 2 years. She had grippe and otitis media twice a few months before. She developed coma in the fourth month of her diabetes. Cold was the precipitating factor of coma. She responded promptly to insulin alone, but although she was only two years old, 125 units of insulin were required in ten hours.

get "sick at the stomach" and start to vomit. Abdominal tenderness can frequently be elicited before they drift into unconsciousness. Is this tenderness a pancreatic tenderness, due to the affection of the pancreas, or is it just a plain abdominal tenderness? Both views will be found expressed in the literature. In a nondiabetic individual after a siege of vomiting, abdominal tenderness can be elicited, for the muscle spasms produced by vomiting are enough to produce "soreness" in the abdominal area.

The immediate cause of vomiting is the state of ketosis which has been pyramiding and has upset normal function. Digestion ceases (for food taken in the last 24 to 48 hours can be found in the gastric contents), acid in the stomach increases, distension of the stomach often occurs and nature's attempt is to get rid of the aggravating situation through vomiting. Frequently hyperpnea is present and later the abdomen always is rigid. The vomitus is often of the coffee ground type and a rapid loss of weight occurs. The child looks very sick during severe acidosis, but so does a nondiabetic individual who is attacked by a severe vomiting spell. The degree of drowsiness is not a good index of the state of such a child. One can be easily deceived if he depends on this as a guide. If hyperpyrexia is present a blood culture should be made to determine the presence or absence of a blood stream infection.

Wagner[3] has stated that a "specific for the coma of childhood is the spotted, sometimes true petechial rash" described originally by Herbert Koch. I have not noticed this and American authors have not stressed this point.

The air hunger can be extreme so as to cause a "tirage" such as is seen in laryngeal diphtheria or other obstructions of the larynx as described by Lemann[4] in a case of a young girl about thirteen. While she was in this condition, says the author, she was seen by a physician whom she had never previously consulted and who was ignorant of the numerous warning signals of the disease which has been present for nearly a year. His first impression of her condition was that there must be some laryngeal obstruction, and it was only after a laryngoscopic examination had proved negative and after he had made a urine examination that the proper diagnosis was established.

Hamburger[5] writes of a child eight years of age, apparently in the best of health who was attacked by severe abdominal pains and was about to be operated on for appendicitis when it was noted that she was breathing deeply. The urine was examined and found to contain sugar. The child died in coma the next day. In my experience it was a boy who developed abdominal pains, was operated on for appendicitis in a small town, the appendix was normal and the boy died next day in coma.

CLINICAL PICTURE, PATHOLOGIC PHYSIOLOGY AND TREATMENT

In diabetic coma, the primary factor is diabetic ketosis, which requires prompt and adequate treatment. First of all, the metabolism of the patient should be reduced to the lowest level possible, which can be accomplished by putting the patient to bed and preserving the heat by the application of warm blankets and the careful application of external heat. The provision of a good nurse who will spare the patient any exertion is essential.

The body is desiccated. Adequate fluids must be given, subcutaneously, intravenously or by mouth if possible. From one and a half to four liters of liquids in twenty-four hours, depending on the age of the child, should be given. Usually it must be administered parenterally as the patient is either too sick or unconscious to take it by mouth. A solution of 10 per

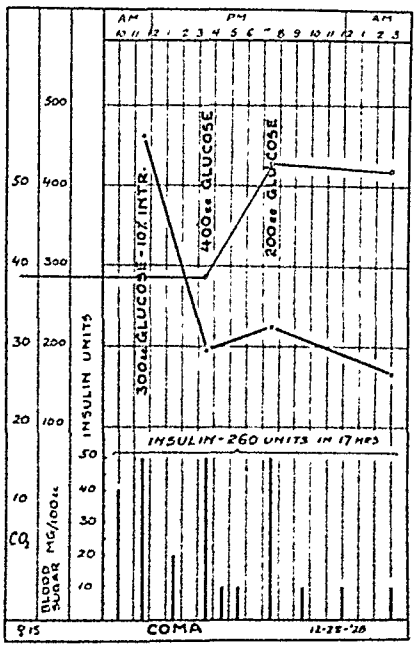


Chart 4. Case No. 2546. A Gentile girl who developed diabetes in 1928, when the diabetes was first recognized by her family physician when she was found in coma, at the age of fifteen years. She had always been in good health, an athletic type of girl. Coma followed rapidly an attack of intestinal "flu". Two hundred and sixty units of insulin were used in seventeen hours together with intravenous glucose. In 1932 she went into coma the second time following a cold. In spite of this she is still mildly diabetic and for months at a time the diabetes was controlled without insulin. She was married in 1933.

cent glucose made up in normal sodium chloride for intravenous use and 3 to 5 per cent glucose in saline for hypodermoclysis, 250 to 500 c.c. given every four to six hours throughout the day or until the patient is conscious and able to take large quantities by mouth. In this connection I have found that orange juice given by mouth is not tolerated well; lemonade, ginger ale, or grapefruit juice made up as a drink and sweetened with sugar is much better. For some reason orange juice tends to increase the nausea in these patients. A Murphy drip of normal saline is another valuable method of crowding in liquids. This should be preceded by an enema in order to clear the lower bowel.

On the whole an attempt is made to convert the metabolism into a carbohydrate one. This is accomplished much more easily in thin patients than in the fat ones. Lipemia is present at times and likely more often a masked lipemia may be present. This is eliminated largely by insulin and by the restoration of normal metabolism with insulin, carbohydrate and saline. If the pulse is weak or irregular, the intravenous medication should be given with care, in smaller amounts, and slowly. In such a case hypodermoclysis or the Murphy drip is preferable. Caffein sodium benzoate or digitalin and the insulin should be given in the glucose which is being administered.

Gastric lavage is often very helpful but it is not indicated in all cases routinely. If the patient appears nauseated and the heartbeat is rapid, this speaks for a distended stomach and in such instance gastric lavage should be performed, leaving the last bulbful of this alkaline fluid in the stomach. In a moribund patient lavage is not a safe procedure.

High colonic irrigation with tenth normal sodium chloride or sodium bicarbonate is a good procedure. The use of alkalies by mouth in small doses is advocated by Boyd[5] and Wagner.[9] Joslin seriously objects to the use of alkalies but the general consensus of opinion is that in small doses they can be given with safety, and are often helpful. In massive doses alkalies are to be condemned.

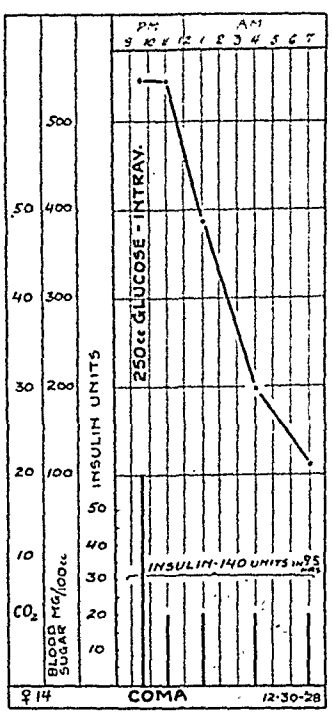


Chart 5. Case No. 2478. A Gentile girl who developed diabetes in 1928, two months before I saw her, at the age of 14 when she was brought in in coma. Coma followed indiscretion in diet and a cold. She had a heavy lipemia. One hundred and forty units of insulin were used in nine and a half hours together with one intravenous administration of glucose. She proved to have a very severe diabetes, difficult to control.

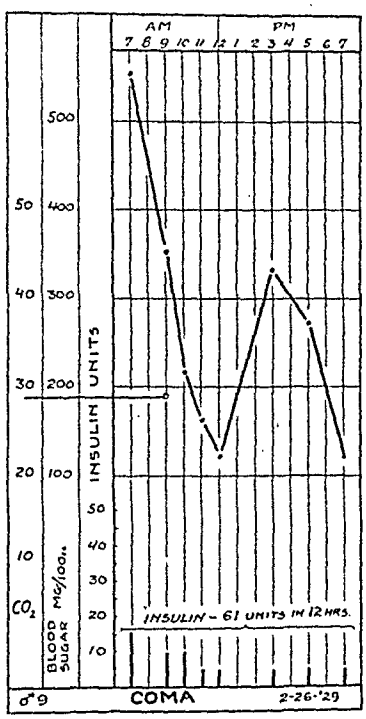


Chart 6. Case No. 676. A Gentile boy developed diabetes in 1924 at the age of 5 years following a sore throat. He did well, had a tonsillectomy in 1925 following which there was a marked improvement of his diabetic condition and a marked reduction in insulin requirement. In 1929, at the age of nine and in the fifth year of his diabetes he went into coma. Only 61 units of insulin were used in twelve hours and the response was good on insulin alone. His diabetic condition, however, was much aggravated after the coma and whereas he had a normal blood sugar for some time up to the onset of coma, following this the insulin had to be markedly increased up to 60 units per day in five or six doses, his blood sugar level stayed high for several months dropping later to a normal level. In 1930 he went into the Cunningham tank for a year, and, ever since, to this date, his blood sugar is very high.

The circulation must be supported. Boyd[5] advocates the alternate use of digitalin and caffeine sodium benzoate, every four hours. I have always used them in the intravenous glucose solution routinely. If shock or collapse occurs the intravenous administration of 10 per cent glucose made up in normal saline, or saline hypodermoclysis are helpful in restoring the blood volume. In exceptional cases a transfusion may be indicated. I had to resort to this procedure but once. Even adrenalin or ephedrin may have to be given.

The best treatment of diabetic coma, however, is its prevention, by adequate treatment by diet or diet and insulin and the removal of all foci of infection. One can protect the individual from the accidental infections which they contract and which can and do precipitate acidosis quickly. There it is necessary to deal with the problem. A fat diabetic patient is a poor risk in coma; one who is thin has a much better chance of recovery.

Brown and Graham[11] report that in the Royal Hospital for Sick Children, of 300 nondiabetic children admitted, 54.7 per cent had acetone bodies in the urine. They placed some of these on a ketogenic diet and found an increase of from two to forty times of acetone in the blood. The administration of dextrose resulted in a rapid diminution of blood and urine acetone. They state that soda bicarbonate can not be depended upon to reduce the acetonemia but it does increase the alkali reserve.

Some damage is wrought in the kidneys during diabetic coma as evidenced by the presence of albumen,

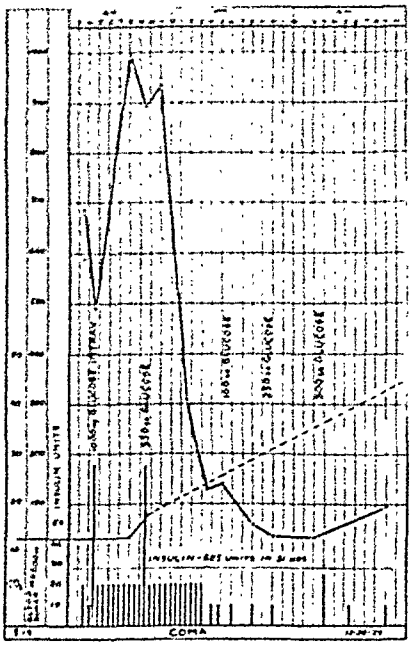


Chart 7. Case No. 1381. A Jewish girl developed diabetes in 1926. The onset of diabetes was preceded by a bad cold with fever which lasted a week. She had a severe case of diabetes requiring 20-20-20 units of insulin per day. In the third year of her diabetes she went into coma because she discontinued her insulin. In the first thirty-one hours 685 units of insulin were used with intravenous glucose and the blood sugar level reached nearly 1000. She got along well, the diabetes is reasonably controlled at present and the patient is a picture of health.

casts, and a high level of urea nitrogen. The postmortem findings also confirm this. Fortunately, the impairment of kidney function represents but a transitory phase in diabetic coma. The chief cause of the renal condition is the damage done by the acetone bodies. This, however, may not be the only factor. Rabinowitch[12] calls attention to the fact that the patient in coma with urea retention may go on to a complete recovery in a few days or there may be in some cases progressive impairment, leading to uremia.

Thus, in any diabetic child carbohydrate tolerance is decreased in the presence of an infection. This can be combatted in one of two ways: either decrease the food intake by one-third, leaving the insulin the same, or else leave the intake the same and increase the insulin. During infection the carbohydrate metabolism must be increased by one of these means. Whether or not the child eats, makes no difference, for the metabolism goes on just the same, insulin is required to insure the combustion of the food. Most catastrophies occur just on this point. The child is not eating, and either the family or the doctor discontinues the insulin, in fear of insulin shock, acidosis increases and the child drifts rapidly into coma.

One can not depend always on the examination of the urine for the ketone bodies for these can be masked even in the presence of severe ketosis. Thus, Feinblatt[13] reports a fatal case of coma in a girl nine years of age when only an insignificant ketonuria was found in spite of extreme acidosis (CO_2 14.3 per cent). A large amount of acetone was present in the spinal fluid and was absent in the blood. Lemann[10] also reports coma without ketonuria; his patient died. This

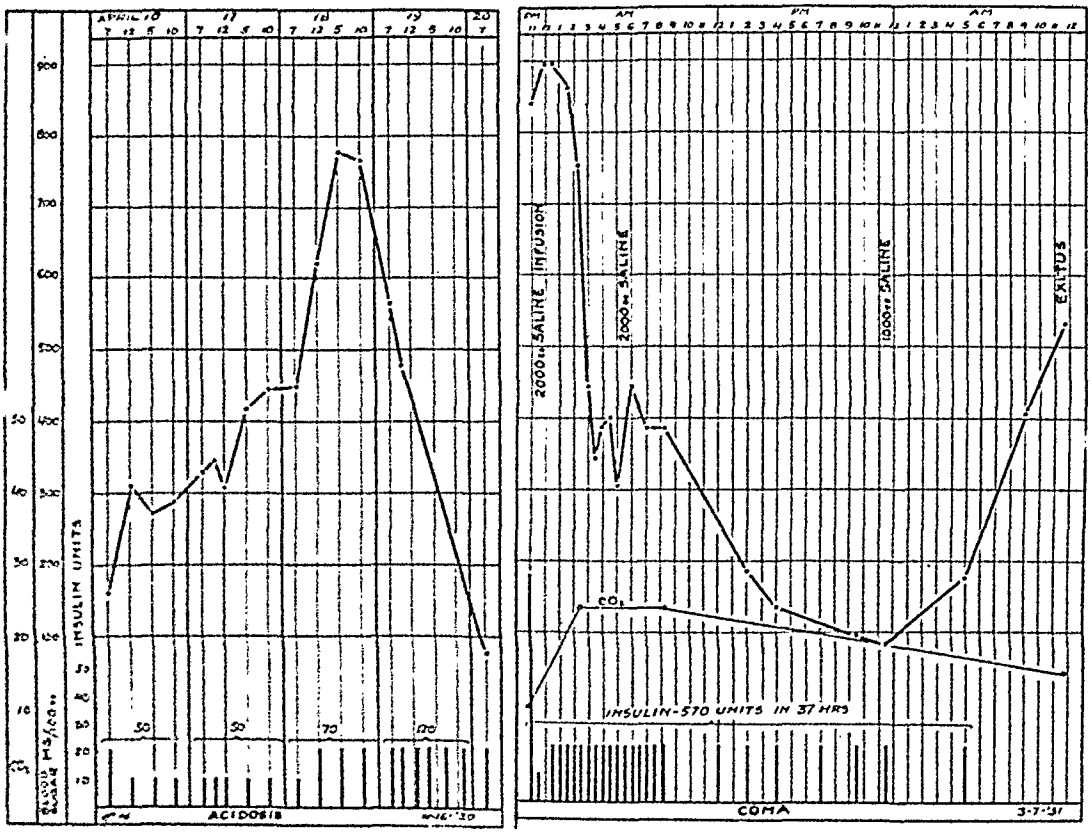


Chart 8. Case No. 2847. A Gentile boy developed diabetes in September, 1929. I saw him first 9-10-29, when he was fifteen with a blood sugar of 880. He responded well to treatment and I was able to carry him on 10-10-10 units of insulin. April, 1930, he had severe acidosis because he had discontinued all insulin. Insulin had to be increased to 120 units a day before the blood sugar level came down. After that his diabetic condition was much aggravated and he needed 20-20-20-20 units of insulin. In March, 1931, he was brought in in deep coma, having been in it for two days and he died on the second day after admission. In spite of 570 units of insulin in 37 hours the CO_2 level did not rise appreciably.

fortunately is not the rule but merely the exception.

In diabetic coma there is also a depletion of the chlorides. This is even more marked if the patient has been vomiting. These must be restored in order to reëstablish a normal, physiologic equilibrium. To administer carbohydrate and neglect chlorides may save a patient from an acidosis only to precipitate alkalosis. In Chart 13, I tried to illustrate the state of affairs and the chemical changes involved. It is constructed after the studies of Hartmann and Darrow.[14] The first picture at the left represents the normal, physiologic status. The chlorides and the bicarbonates, in terms of tenth normal acid, occupy the large portion and their relation is fixed and constant. The second figure shows what happens in diabetic ketosis. The chlorides and the bicarbonates are both decreased in amount and the ketone bodies occupy a portion of the space which the former would occupy normally. If large quantities of glucose and insulin are given, changes such as are demonstrated in the third figure occur. The ketones have gone, the bicarbonate has increased beyond its normal space and has crowded some of the chloride out and alkalosis is the result. If, however, sodium chloride is administered with the glucose and insulin in the form of normal saline, the chlorides are increased as the ketones are decreased and the rather labile bicarbonate appears at its normal level. One or two administrations of glucose-saline-insulin are usually adequate in most cases. If vomiting persists then this must be continued longer. In case no saline had been given, but just the glucose and insulin, and the coma deepens, the respirations become prolonged, always suspect alkalosis and in such a case 2 to 4 grams of ammonium chloride may be given by the stomach tube, with plenty of water.

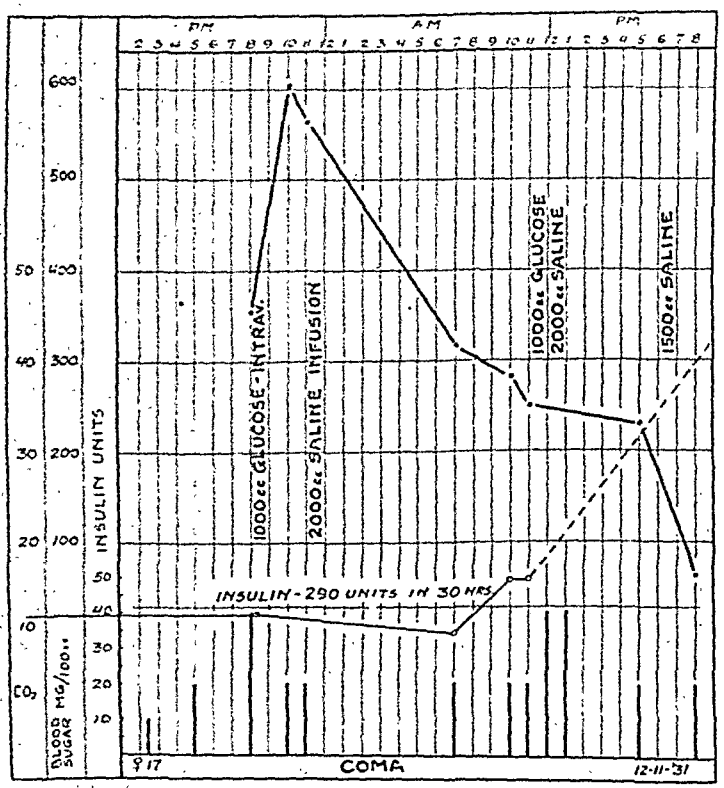


Chart 9. Case No. 3872. A Gentile girl developed diabetes in 1927 at the age of 13. I saw her first in 1931, when she was brought in in deep coma, in the fourth year of her diabetes. She refused to take insulin when her diabetes was first discovered and she did not adhere to diet, consequently went into coma the first time in 1928. In thirty hours 290 units of insulin were given together with intravenous glucose with a good response in a girl 17 years old. She is a picture of health, a dancer, but requiring a heavy insulin dosage, 20-20-20.

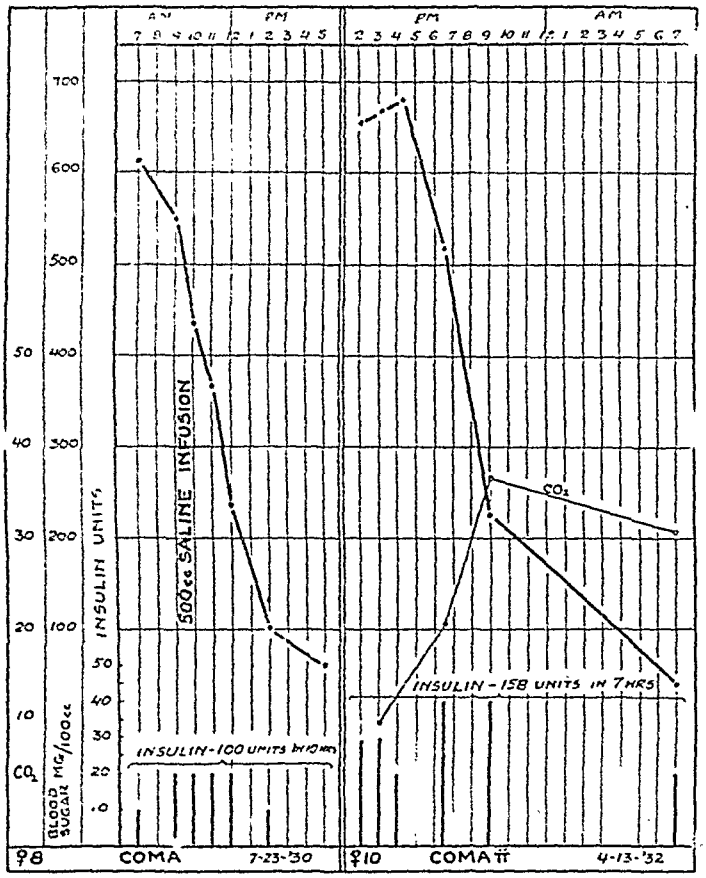


Chart 10. Case No., 713. A Gentile girl who is one of the youngest diabetics I have had under my care, having developed diabetes at the age of fourteen months in January, 1924. A cold preceded the onset of diabetes. The onset of coma, in 1930 at the age of eight, followed an attack of whooping cough and few days after a cold. One hundred units of insulin were used in ten hours together with intravenous glucose with a prompt response. Her progress following coma was good. In February, 1932, she had chickenpox and in April of that same year she went into coma the second time at the age of ten years. One hundred and fifty units of insulin were used in seven hours with a prompt response. Blood sugar levels were high both times.

While the administration of liquids is very important, the dosage of insulin also must be adequate. It is better to give smaller doses of insulin, 10 to 20 units, every half to one hour, than to give large doses every few hours. Insulin should be given as soon as the diagnosis of coma or severe acidosis is made. I have given patients insulin intravenously right in my office when they come in severe acidosis verging on coma, so that even the hour or so between the office and their entrance to the hospital would not be lost. Time counts. Insulin given intravenously acts more quickly than insulin given hypodermically and the first few doses should be given by the intravenous route. When giving glucose intravenously, it is incorporated into the solution. If given with glucose, I usually use 25 to 50 units per dose, whether 250 or 500 c.c. of the solution is given. Hourly blood sugars, acetone and bihourly determinations of carbon dioxide combining power enable one to judge accurately the progress of the patient and point the way of the rate and size of insulin doses. At first, insulin can be given every half hour, but as soon as the blood sugar level reaches a level of 250 or so, one must proceed with caution. If blood studies are not available the regimen must be regulated by the urine examination of sugar and acetone and if the patient can not void, catheterization should be resorted to every two hours. Blood chemistry is much easier and much more specific. If one pro-

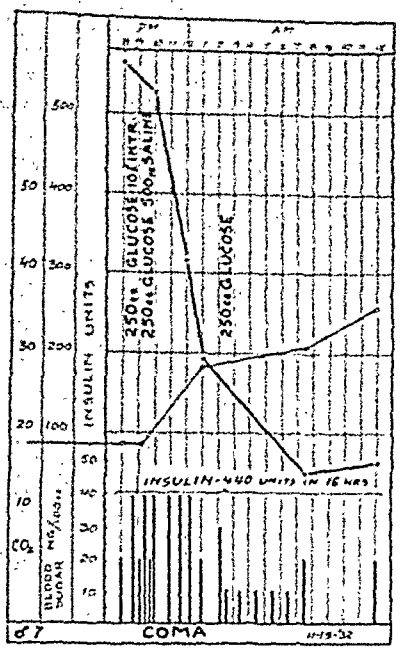


Chart 11. Case No. 3893. A Gentile boy who developed diabetes in 1931 at the age of three years. This was preceded shortly by chickenpox. Along with diabetes he had asthma. He proved to have a mild case and he was treated by diet alone and later on only 5-5 units of insulin. Finally all insulin was discontinued and he had a normal blood sugar level morning, noon and night. In November, 1932, at the age of seven and in the fourth year of his diabetes, he went into coma because of indiscretion in diet. In sixteen hours 440 units of insulin were given together with intravenous glucose with a good response. He has done well since and is taking at present 18-18 units of insulin per day.

ceeds at this speed, in the course of two to four hours the patient's condition is usually controlled.

In case the patient has vomited coffee ground material this is a definite evidence of dilatation of the stomach which should be washed out with a weakly alkaline solution and when the washings come clear, leave the last bulbful of this alkaline water in the stomach. The liquid naturally should be quite warm. In a patient who is or has been vomiting, there is a depletion of chlorides.

I have always preferred using "Bi-So-Dol" as the alkali of choice. In children especially, when this is given in hot water (never in cold water) it has a pleasant taste and the children do not object to it. A moderate use of alkali is a good routine; massive doses of alkali are objectionable as they are apt to produce vomiting and are not necessary anyway. Alkalies should never be given intravenously or hypodermically.

THE MECHANISM IN DIABETIC COMA

The mechanism in diabetic coma, the so-called "shock theory" has been the subject of intensive investigation in recent years. The factors involved have been studied intensively by Atchley[15 16 17] and Peters[18 19 20 21] and their co-workers. I am taking the liberty to give a brief summary of their important work after Lande:[22]

"The breakdown of carbohydrate metabolism causes a greatly increased water excretion and an equally pronounced excretion of electrolytes normally present in the intracellular and extracellular fluids, particularly sodium and potassium. With the onset of acidosis, the excretion of ketones greatly augments the loss of water and electrolytes. As a result of the rapid loss of water, sodium and potassium, there develops a depletion of base in the body sufficient to cause dehydration of tissues, the alkali deficit becomes more marked and hyperventilation ensues with its tendency to depress blood pressure. There develops, at the same time, an increased permeability of the capillary walls with the tendency of fluids to pass from the vessels into the tissue spaces. In mild forms the transudate is relatively free from proteins, but in severe grades of acidosis permeability is so altered that proteins pass with the fluids from the blood stream. The diminished blood volume, lowered blood pressure, capillary stasis and escape of fluids from the blood stream combine to produce the syndrome of shock.

"During acidosis the blood is inspissated, as indicated by the normal or high serum protein and hemoglobin and the lowered blood volume. The depletion of plasma fluid is due not only to diuresis, vomiting and hyperventilation but also to loss of fluid through the capillary walls. Recovery in part involves the restoration of serum volume, but to a certain degree serum volume and body fluid act as independent variables and the replenishment of body fluids does not necessarily result in restoration of blood volume. Circulatory failure, particularly peripheral stasis, is responsible for the escape of fluids from the circulatory system and for the failure to remain in or return to the vascular bed. Such circulatory failure can develop when carbohydrate metabolism is proceeding in a satisfactory manner and the serum carbon dioxide is rising. In the production of coma, ketosis and alkali deficit play an indirect role by producing diuresis and overventilation. If shock is an important factor the restoration of the blood volume becomes an essential aim of treatment and the blood protein figures as a measure of hemoconcentration and the blood pressure are as important as the blood sugar and the carbon dioxide of the blood in directing treatment.

"Clinically, hemodilution seems to mark improvement. Delay in restoration of serum volume and hemoconcentration is associated with the continuance or increase of symptoms. Cases are cited in which the blood protein figures were a more accurate reflection of the clinical picture than either the blood sugar or the blood carbon dioxide. In one instance cited by Peters the patient remained in profound coma with a carbon dioxide combining power of the blood well above the critical level. The liberal administration of fluid restored consciousness without significant change in the blood carbon dioxide or the blood sugar, but with a marked decrease of blood protein."

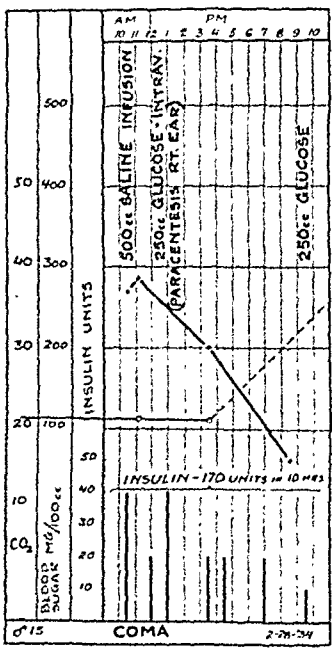


Chart 12. Case No. 886. A Gentile boy whom I first saw 3-24-25, at the age of seventeen months with recent diabetes and in acidosis. He made good progress and got along at first on a small dosage of insulin. Later this had to be increased and he was in acidosis several times. In 1926 he had a tonsillectomy, following which his diabetic state improved. He developed bronchopneumonia in December, 1926, and otitis media followed. After this his diabetic condition became worse. Another otitis media in 1927. In 1934, at the age of thirteen and in the eleventh year of his diabetes he was brought in in coma. This followed an attack of otitis media which was preceded by a sore throat. In ten hours 170 units of insulin were given together with intravenous glucose and parecentesis was performed. His recovery was uneventful.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis in the presence of coma may cause at times some difficulty or at any rate require time for the clearing up of the problem. Blood counts are of little or no value, for in diabetic coma there is dehydration, with concentration of the blood and for that reason blood counts are high.

Hypoglycemia due to an overdose of insulin is often encountered. Coma due to diabetes presents desiccation, a dry tongue, a forced "Kussmaul type" of breathing. A hypoglycemic coma presents none of these; the patient breathes easily, he is usually drenched with perspiration, the onset is rapid, whereas in diabetic coma it is gradual. The history of last insulin having been given from one to three hours previously can usually be elicited. Blood sugar is high in coma, whereas in insulin shock it is low as a rule. It can also be high, for I have seen a case of insulin reaction with a blood sugar of 364. When one is uncertain which problem of the two one is dealing with, give always 5 to 10 c.c. of a 50 per cent solution of glucose intravenously; if it is hypoglycemia the patient will be conscious in five to ten minutes and the problem is settled: if it should be diabetic coma, no harm has been done by this measure.

A rise of temperature is an important sign. Fever is not an accompanying symptom of diabetic coma. In such a case look for infection, otitis media or a gastrointestinal upset. In any diabetic patient who has fever in the presence of acidosis, one must look for septicemia. Repeated blood cultures are necessary, for the first one may be negative. One every two days should be taken until a positive culture is obtained or until the possibility of septicemia is definitely ruled out. Infections such as carbuncle, gangrene or an infected wound should always be accompanied by blood cultures. If fever or chills result after a tooth extraction a blood culture should be done, for septicemia may be present. If an operation is done, for instance for a carbuncle, a blood culture should always precede the operation so as to protect the surgeon, and also enable the physician to give a timely warning as to the prognosis. Often the acidosis resulting from an infection is not sufficient to cause coma and the real cause of the patient's comatose state is the septicemia due to staphylococcus or streptococcus infection. The finding of septic temperature, leucocytosis,* petechiae of the skin, subconjunctival hemorrhages, metastasis to the joints, lungs and endocardium or sweating often remove doubt as to the diagnosis.

Meningitis and encephalitis usually offer evidence of irritation of the central nervous system. The history of headache, dizziness and drowsiness for a week or more, fever, pupillary changes, nystagmus, paralysis, stiff neck, reflex changes and stertorous respiration rather than "air hunger", says Root,[23] indicate that a lumbar puncture should be made to settle the diagnosis.

Trauma with concussion of the brain or a fractured skull must be thought of when a patient is found unconscious with sugar and diacetic acid in the urine for

*This is a relative term. In order to evaluate it estimate the corpuscle volume or do a red cell count. If these are high, then leucocytosis is of little value; if normal then leucocytosis has a definite diagnostic value.

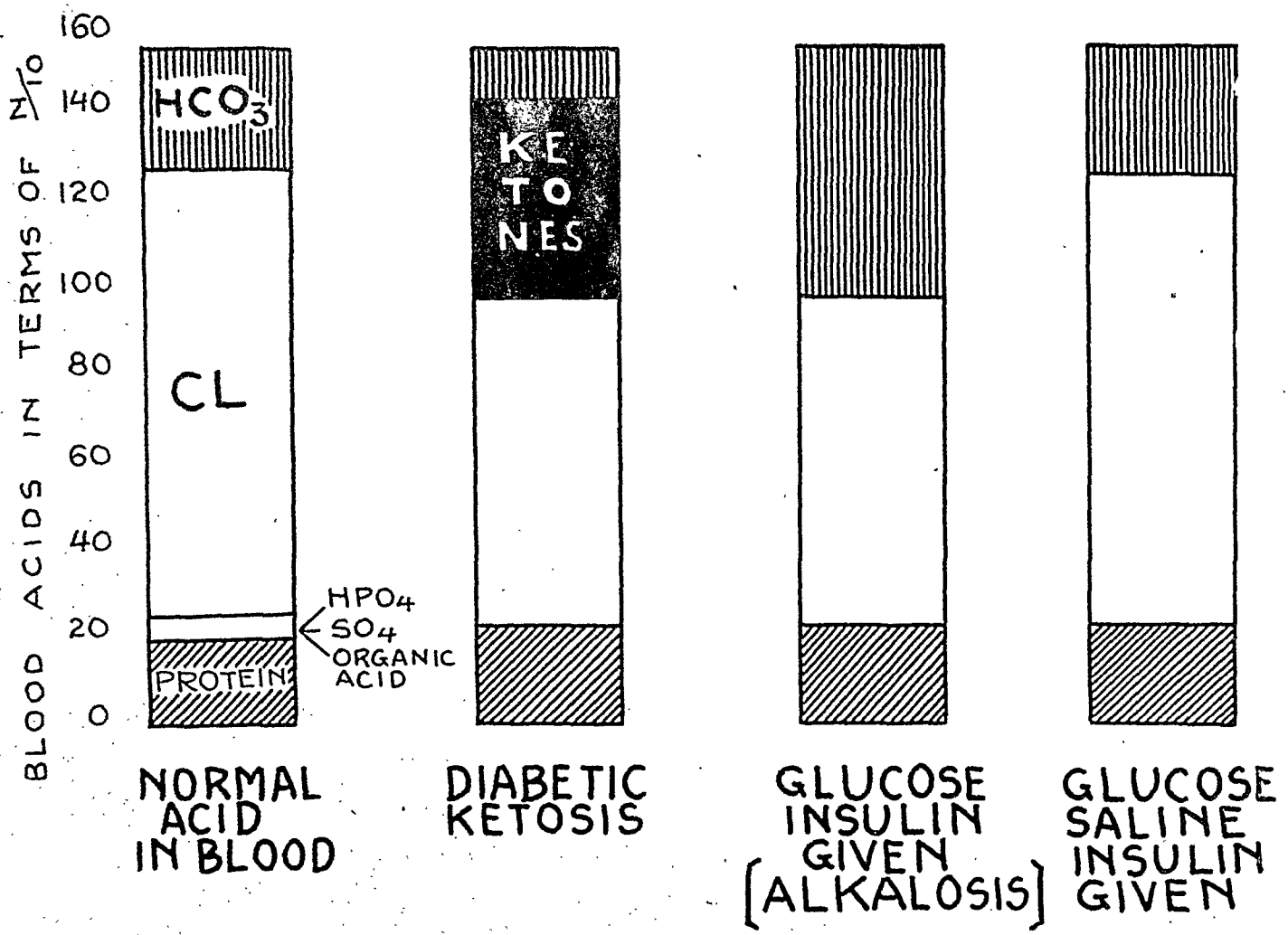


Chart 13. A schematic representation of diabetic ketosis and the changes after a. glucose-insulin and b. glucose-insulin-saline. /Reconstructed after Hartmann and Darrow.

such a patient need not be necessarily suffering from diabetic coma. Bleeding from the ears or nose, wounds of the scalp, roentgenograms and blood chemistry help to differentiate the condition.

SUMMARY

1. In a group of 218 children (first and second decade) there were fifty instances of coma.

2. Of the thirty-one children who were under my immediate care during coma, five died. Three of these were moribund when they arrived and died one hour after admission. One died in the pre-insulin era. One died on the second day of cardiac failure.

3. Of the nineteen children from my series of 218 who were treated by the family physician during coma, sixteen died and three survived.

4. The sex incidence of coma in diabetic children is practically evenly divided: twenty-seven boys and twenty-three girls.

5. The total mortality in both groups was twenty-one cases. Of these, eleven were boys and ten girls. Twelve or 57.1 per cent died in their first year of diabetes; 66.6 per cent died during the first two years of diabetes.

6. The differential diagnosis and methods of treatment are discussed.

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ABSTRACTS

RIESMAN, DAVID, AND DAVIDSON, HAROLD S.

Beriberi Following Drastic Voluntary Dietary Restriction. J. A. M. A., 102:2000 (June 16), 1934.

Beriberi is a vitamin B deficiency disease characterized by cardiovascular changes, edema and polyneuritis.

Vitamin B is contained in vegetables, fruits, milk, yeast, kidney, liver, bran and whole grain.

Beriberi presents itself in two distinct forms. In one form the polyneuritis predominates and this type must be differentiated from polyneuritis due to other causes.

In the second form, edema is the outstanding feature. Edematous cases or beriberi generally show pain on pressure over the calf muscles.

Other symptoms complained of in beriberi are: loss of appetite, fullness in the stomach, and nausea and vomiting occasionally. Weakness in the legs is a characteristic and an early symptom, later moderate edema, paralysis of the legs, and general irritability, headache and dizziness develop. Hemorrhagic exudates often appear in the skin. Fever is absent. Palpitation on exertion and dyspnoea are present.

The authors cite two cases, one an old man who voluntarily restricted his diet until he was taking only one and one-half quarts of milk a day over a period of a year and a half. He developed a clinical picture of beriberi.

The second case cited is that of a young woman who adopted a meagre and monotonous diet to reduce her weight. She developed edema of the legs, shortness of breath and palpitations.

The authors point out the best sources of vitamin B for clinical use are yeast and wheat germ. Tomatoes, raw cabbage, fresh spinach and legumes contain more than orange or lemon juice, onions, cauliflower, or lettuce. Milk does not contain a large amount of vitamin B.

Francis D. Murphy.

HARROP, GEORGE A.

A Milk and Banana Diet for the Treatment of Obesity. J. A. M. A., 102:2003 (June 16), 1934.

The banana is a filling food, has a negligible fat content. Milk alone becomes monotonous and flat. Skimmed milk has one-half the caloric value of whole milk.

When used as a continuous diet one or two large ripe bananas may be used with one glass of milk (250 c.c.) for both breakfast and lunch. Evening meal restricted consisting of thin soup, a slice of lean meat (or fish or fowl), two or three portions of a five per cent vegetable, a slice of bread and butter, and a portion of uncooked fruit. Such a diet will contain 1000-1200 calories.

The second method involves using bananas and skimmed milk alone over a period of ten days to two weeks. The strict diet consists of six large bananas and 1000 c.c. of skimmed milk to be eaten in three or more meals. Bananas must be fully ripened. Skimmed milk is obtained by pouring off the top fourth of a quart of milk and using the remainder.

This diet following ten days to two weeks produces a reduction of four to nine pounds in persons who are active.

Fluids without food value as tea or coffee without cream or sugar are permitted freely.

Six large glasses of water a day must be taken in addition to the milk. Salt is restricted.

The diet is simple, cheap, readily available and palatable.

Francis D. Murphy.

GEBHART, H.

The Problem of the Co-called "Renal Diabetes". Arch. f. Verdauungskrankh, No. 56, July, 1934.

Case report of a severe glycosuria with ketonuria following trauma to the skull without augmentation of blood-sugar levels. Patient was resistant to the administration of insulin or carbohydrates. Adrenalin and pituitary injections also responded as in normally sugar-free patients. However, the output of water was increased. There was no pathology of the kidneys and it is assumed that a reduced filtrating power of the kidneys to sugar due to central nervous disturbances was responsible for the glycosuria. It is interesting that the case was considered as a traumatic renal diabetes and therefore was amenable to compensation for sustained injury.

M. E. Gabor (Milwaukee, Wis.).

SECTION IV—*Roentgenology*

X-RAY DIAGNOSIS OF ACTIVITY AND CURE OF DUODENAL ULCER*

By

ALICE ETTINGER, M.D.

and

W. E. DAVIS, M.D.

BOSTON, MASSACHUSETTS

ALTHOUGH numerous excellent articles dealing with the correlation of clinical and X-ray findings in duodenal ulcer have appeared in European literature, American journals show few (1, 2) which are based on the refined technique advised by Akerlund (3) and Berg (4). That compression technique with aimed exposures has not become a routine part of every gastro-intestinal examination, as it has in Europe, is probably due to the fact that no American manufacturer has yet furnished a satisfactory apparatus for its successful application. We need not go into any detailed discussion of different types of apparatus, as quite a few are satisfactory for the purpose. Only two points have to be observed for successful work; they are the possibility of a rapid switchover from fluoroscopy to radiographic work and the possibility of applying compression. Though the "quick switch" device reaches its height of usefulness in gastro-intestinal diagnostic work, it has further application in other fields, such as lungs (5) and gall bladders.

The method which we have used in this study is identical with that advised by Berg, with whom one of us had the privilege of working for several years. We used the latest model of Berg's apparatus.

As is well known, the axis of the duodenal cap in the average case runs from inferiorly-anteriorly to superiorly-posteriorly. Thus the cap with the patient in an antero-posterior direction is seen in a markedly shortened projection. The apex of the cap cannot be separated from the superior angle of the duodenum, and the distal part of the cap is mostly obscured by the descending duodenum which passes behind it. Therefore, the cap always has to be examined in the right-oblique diameter. The lesser and greater curvatures of the cap then form its outline. Only few ulcers will be visible in profile in this position, as most duodenal ulcers are known to be situated on the anterior or posterior wall. Therefore, if a niche is present, it will be seen *en face*. The spot of increased density which represents the *niche* often can be seen only when a certain amount of compression is applied. The amount of pressure must be carefully regulated, as too much pressure will squeeze the entire contents out of the bulb, while too little will not provide enough contrast for definite recognition. Pressure also brings out changes in the mucosa surrounding the niche, namely, an area of diminished density indicating the edema of the mucous membrane or a star-shaped convergence of the folds which indicates the beginning of healing. The ulcer may be seen in profile by examination in the left-oblique diameter, in which position the anterior and posterior walls form the outline of the roentgen shadow. The degree of rotation has to be varied in different individuals, as an ulcer which is situated nearer the *lesser* curvature on the anterior wall will require a greater angle of rotation than one occurring nearer the *greater* curvature, while on the posterior wall the reverse is true. Therefore, it is necessary to observe carefully under the fluoroscope at what particular position the ulcer is seen in complete profile, because, otherwise, comparative studies at intervals would be valueless in determining changes in the size of the *niche*. The edema of the mucous membrane surrounding the niche in this position is represented by a concavity on either side of the *niche* profile.

In discussing the value of this method, some American roentgenologists are inclined to maintain that the method offers nothing new in principle and that all that would be obtained additionally would be a record of the findings which are already secured by fluoroscopic examination. They do not think it necessary for just this adjunct to their diagnosis, to bother with a method which undoubtedly takes some practice and intimate study and slightly prolongs the time of examination. In answer we might bring forward several points. First, we believe that a comparison of size of the *niche* as seen at intervals is of great clinical value and can only be carried out if permanent records are available. Furthermore, two circumstances may make the fluoroscopic diagnosis of a *niche* extremely difficult for the roentgenologist. One of them is the great irritability of a diseased cap which may be so marked that the actual time for perception of the silhouette of the cap will be too short to recognize any details. A quick snapshot, however, makes a record which may be studied and evaluated later. Secondly, while usually the *niche* is represented as an area of increased density, swelling of the mucosa may obstruct

*From the X-ray Department and the Medical Clinic of the Boston Dispensary and the Department of Medicine, Tufts Medical School.
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the entrance to its lumen so much that only a slight trace of barium covers the base of the *niche* and only a very faint shadow of the *niche* results which escapes detection by fluoroscopy. Great difficulty may be encountered in examining very obese persons in whom only a plate taken at the proper angle will reveal the diagnosis. These are all not unusual occurrences but difficulties with which all roentgenologists are familiar in examination for duodenal ulcer.

It is obvious from the foregoing discussion that our primary aim in establishing our diagnosis is to demonstrate the actual anatomical change, namely, the ulcer, with the highest possible detail and as nearly as the pathologist sees it with the naked eye. Everyone will agree that the exact anatomical knowledge, viz., size, reactive changes in the surrounding tissues and localization, may have a very important bearing as to the prognosis of the clinical course of the disease. For example, we know that an anterior wall ulcer is more likely to give rise to the complication of perforation into the free peritoneal cavity, while ulcers on the posterior wall are prone to penetration into the pancreas and gross hemorrhage (6).

Though this is our aim, we do not mean to imply that it is possible in all cases. There still remains a significant percentage (varying with different examiners) in which only the deformity of the cap, first so well outlined by Cole (7) as direct evidence of ulcer, is present. Akerlund (3) was able to demonstrate the *niche* in 75 per cent of his cases. Berg (4) reports the *niche* in over 50 per cent, Albrecht (8) in 90 per cent, Clark and Geyman (1) in 54 per cent, Buckstein (2) in 29 per cent, Carman and Sutherland (9) in 13.7 per cent of 1,658 cases, and Kirklin (10) in 15 per cent. In our series of 48 cases which had clinical symptoms examined during the past year (the total number of duodenal ulcers diagnosed by X-ray during the same period was 60) we were able to demonstrate *niches* in 50 per cent. These statistics are not entirely comparable for two reasons: First, only part of them are based on the same X-ray technique, and second, the selection of the cases presented does not correspond clinically. In some instances the statistics represent cases with clinical evidence of ulcer at the time of examination, which is true of our series of 48 cases. In others, cases are included with deformity found in routine examination without corresponding clinical complaints (Kirklin, 11). Our statistics concern all cases in which *niche* evidence was obtained by radiograph independently of whether accompanying deformity was present or not. The number of cases in which the *niche* is the only demonstrable X-ray finding is, in our experience, larger than usually realized. The statement of Cole (7) in 1914 that "if one radiograph out of fifty shows a perfectly normal cap, a negative diagnosis of post-pyloric ulcer is justified," certainly is no longer true. If then the X-ray technique of diagnosing duodenal ulcer has changed so markedly, it is not surprising that the view of the possibility of determining the activity of duodenal ulcer by X-ray must also undergo a change.

We will present five cases from our series which illustrate certain factors in the correlation of clinical and X-ray findings in the course of the disease and the part that X-ray findings may play in determining the activity of the lesion.

Case 1—D. A. B. 28 years. White. Male. For several months he had had moderate epigastric distress and pain radiating to the back, coming on 1 to 2 hours after meals and relieved by food and soda bicarbonate. Gastric analysis showed hyperchlorhydria. X-ray examination without compression showed an apparently normal duodenal cap but under compression a well-defined niche could be seen on the anterior wall (see Figs. 3 and 4) and the stomach showed marked gastritis.

He was placed on an ambulatory Sippy *regime* with almost complete relief of symptoms within a few days. Re-examination 6 months later, at which time patient complained of occasional distress if not careful of his diet, showed disappearance of the *niche*. At the site of the previous niche, star-shaped convergence of the folds was seen and definite deformity of the cap had meanwhile developed (Fig. 5). The stomach still showed gastritis.

Case 2—D. F. 39 years. White. Female. For five years she had had intermittent spells of epigastric soreness and aching pain, at times becoming severe and radiating to the back, often associated with nausea and occasionally vomiting. The pain was helped by heat but not by alkalies and she never ate while it was present. It usually occurred 2 to 4 hours after meals but not after every meal. Symptoms persisted for several weeks with intervals of several months freedom from symptoms.

Gastric acidity was normal. Graham test showed normal gall bladder. X-rays of stomach and duodenum showed a deformed duodenal cap with a small *niche* seen on the posterior wall (Fig. 6).

On ambulatory treatment, she was completely relieved and re-examination nine months later showed disappearance of the *niche* but the cap was still deformed (Fig. 7).

Case 3—L. R. 33 years. White. Male. He had had epigastric distress 1 to 3 hours after meals for six months with occasional nausea and vomiting. Food or alkalies gave relief. He had lost 11 pounds in weight. Three years before there had been similar symptoms for several months which disappeared without treatment.

X-ray studies showed a well-defined *niche* on the anterior wall of the cap (Figs. 8 and 9). Control examination after three weeks hospital treatment, patient clinically relieved, showed *niche* still present but somewhat smaller. When examined again three months later, still symptom free, X-rays showed an apparently normal cap in the first diameter but a definite *niche* was seen in the second diameter at the same site as previously (Figs. 10 and 11). A fourth examination nine months after institution of treatment showed complete disappearance of the niche and the cap constricted at the point where the *niche* had been seen. The patient was symptom free.

Case 4—T. J. T. 55 years. White. Male. He gave a history of recurrent spells of epigastric pain for a period of over 15 years. Pain occurred 1 to 2 hours after meals and was relieved by food or alkalies. At first the spells occurred at intervals of a year or more but more recently every few months. There was occasional vomiting but never hematemesis or melena. X-ray examinations with complete filling at intervals during 15 years had shown persistent deformity of the first part of the duodenum but a *niche* was never visualized.

In September 1933 his symptoms recurred and no relief was obtained by ambulatory treatment. X-ray examination of the stomach and duodenum showed a well-defined *niche* on the anterior wall of a deformed duodenal cap (Fig. 12).

He was then placed on hospital treatment with complete relief of symptoms after the first week. The stools at first showed occult blood but this disappeared after 11 days. After three weeks of hospital treatment, control examination showed the *niche* persisting though apparently slightly smaller (Fig. 13).

A week after leaving the hospital the distress recurred and two weeks later the ulcer perforated. At operation the perforation was closed and he made a satisfactory operative recovery but symptoms persisted for two months.

Case 5—W. B. 26 years. White. Male. For six months he had had epigastric pain with characteristic food relationship. There was a history of periodic spells of the same nature for five years and three years previously a constant deformity of the duodenum by X-ray was reported. Stools showed occult blood.

X-ray examination showed a *niche* on the anterior wall of a deformed duodenal cap (Figs. 14 and 15).

On strict medical treatment in the hospital, he became symptom free after one week and after two weeks the stools were free from occult blood. However, control X-ray examination after three weeks' treatment showed the *niche* still present although definitely decreased in size. After discharge he remained symptom free. A third examination six months later showed complete disappearance of the *niche* while the deformity persisted (Fig. 16).

In Cases 1 and 2, there is a complete correspondence between clinical and X-ray findings. In the other three cases control X-ray examinations demonstrated continued activity of ulcers where there had been disappearance of symptoms for several weeks. In Case 4, the persistence of the niche after treatment and its localization on the anterior wall led us to keep this



Fig. 1. Fold relief of the normal duodenal cap as seen in the right oblique diameter. Arrow indicates pylorus.

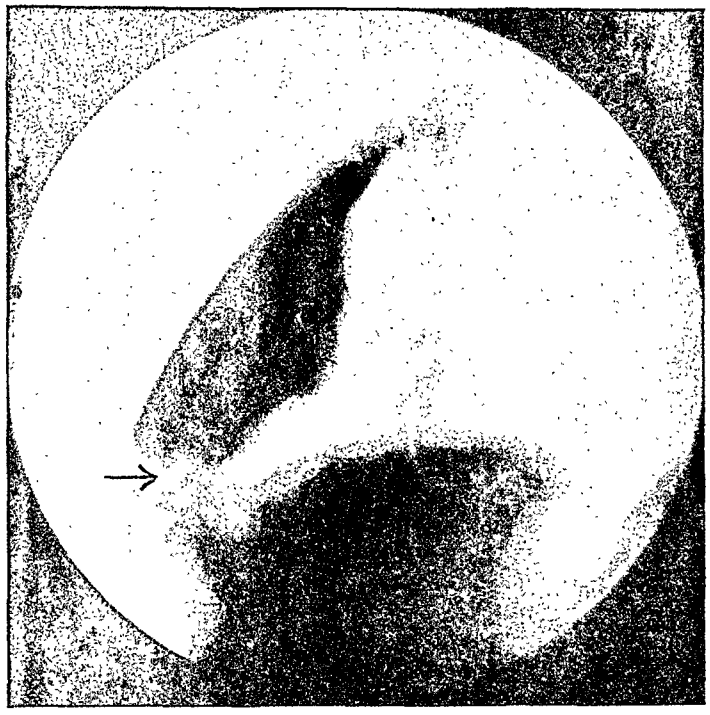


Fig. 2. Cap seen in the left oblique diameter.



Fig. 3. (Case 1) Duodenal cap in the right oblique diameter without compression showing an almost normal appearance.



Fig. 4. (Case 1) Same as Fig. 3 with compression showing a definite niche with surrounding edema. Arrow indicates plyorus; Double arrow indicates niche.



Fig. 5. (Case 1) Appearance of cap six months later, showing a star shaped convergence of the folds toward the spot of the previous ulcer, and typical deformity.

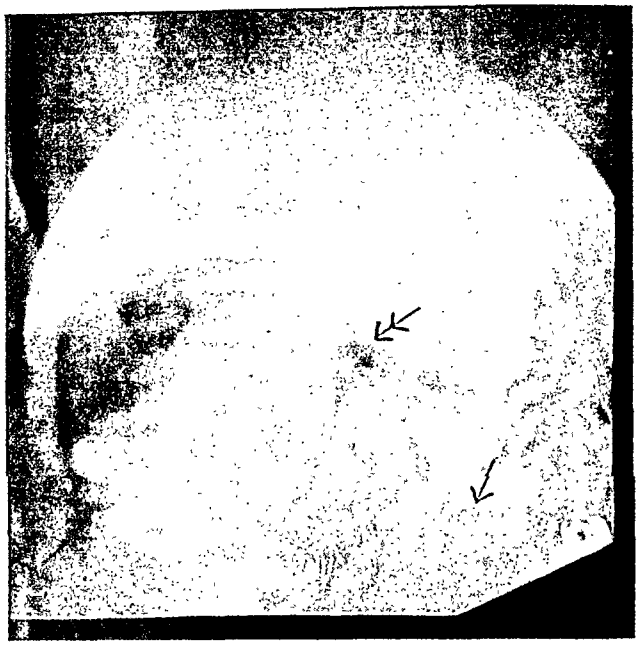


Fig. 6. (Case 2) Duodenal cap in the right oblique diameter showing butterfly wing deformity and pin point niche.



Fig. 7. Appearance of same after 9 months' treatment showing disappearance of niche with persistent deformity.



Fig. 8. (Case 3) Duodenal cap in the right oblique diameter showing a large crater just behind the pylorus. Note the marked area of diminished density around it representing swollen mucosa.



Fig. 9. Same as Fig. 8. Cap in the left oblique diameter showing niche on the anterior wall in profile surrounded by double concavity representing the profile view of the swollen margin of the niche.

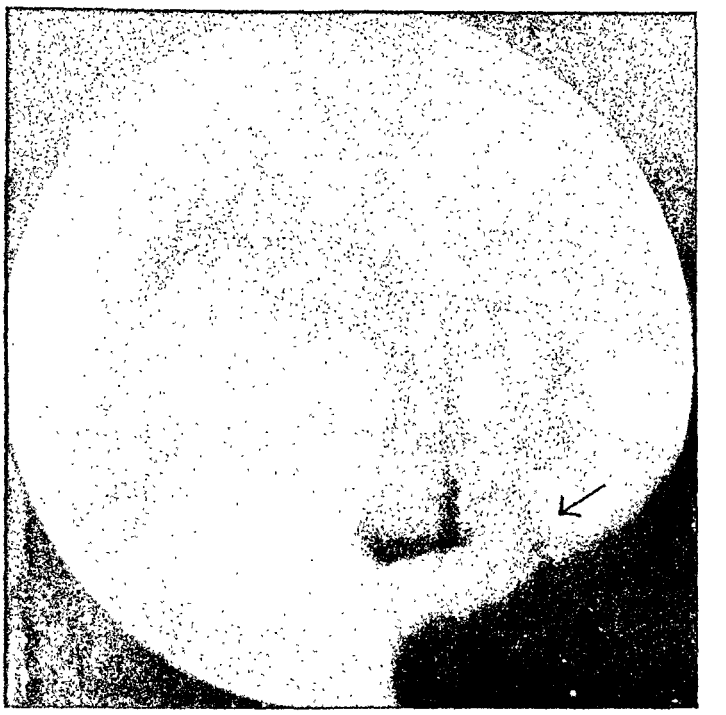


Fig. 10. (Case 3) Appearance of cap as seen in the right oblique diameter after 3 months' treatment showing only broadening of the folds, but no niche.

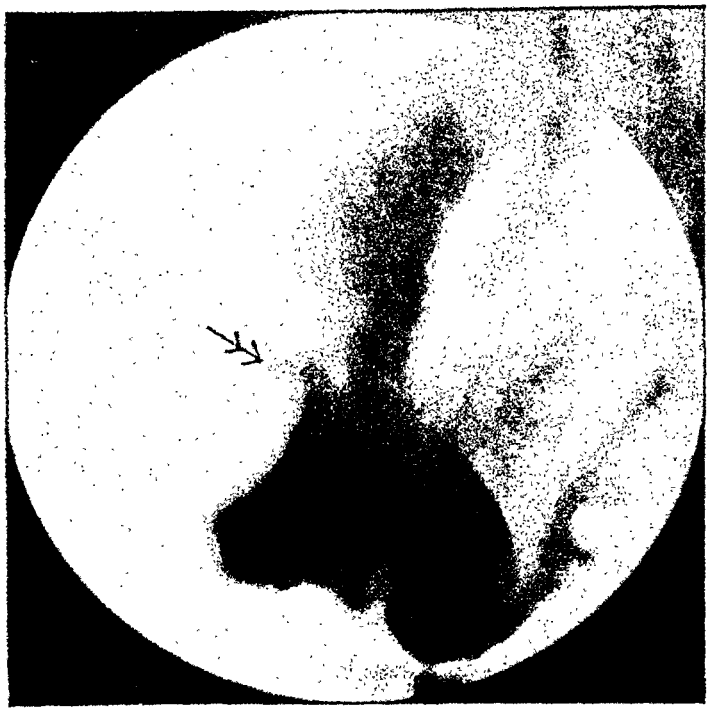


Fig. 11. (Case 3) Same as Fig 10 except in the left oblique diameter. In this position the anterior wall niche can still be easily recognized.



Fig. 12. (Case 4) Duodenal cap as seen in the left oblique diameter, showing typical anterior wall niche.



Fig. 13. (Case 4) Same after three weeks' treatment, showing decrease in size of niche.



Fig. 14. (Case 5) Duodenal cap in the right oblique diameter showing large niche *en face* near the lesser curvature.

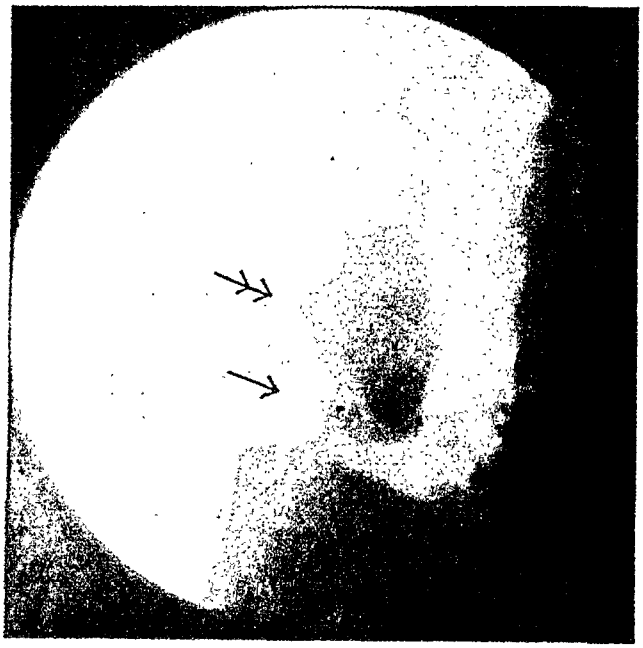


Fig. 15. (Case 5) Same as Fig. 14 as seen in the left oblique diameter showing the position of the niche on the anterior wall.



Fig. 16. (Case 5) Same as Fig. 14 taken after six months' treatment. Niche has completely disappeared, but the deformity persists.

patient under close observation and the subsequent perforation was not wholly unexpected.

The cases reported are given to illustrate what has been our frequent experience in comparing clinical and X-ray findings in duodenal ulcer, namely, that while in most cases institution of satisfactory treatment is followed within a week by complete relief of symptoms, X-ray examination within six weeks usually shows little change (Cases 3, 4 and 5). Later control examinations show X-ray evidence of healing (Cases 1, 2, 3 and 5). These observations are in agreement with Albrecht (8). He followed 165 patients with duodenal ulcer who underwent hospital treatment. "The result of the treatment was as follows:

Clinically without symptoms	76	46.1%
Clinically improved	72	43.6%
Unchanged	17	10.3%

"Out of the 165 duodenal ulcer patients, 83 patients (50.3%) were controlled by X-ray examination after the treatment. In the control examination, the *niche* which had been demonstrated in all the cases before treatment had

been changed into a scar	15	18.1%	(46.1%)
decreased in size	24	28.9%	(43.6%)
unchanged	44	53.0%	(10.3%)

"The percentages of clinical success of treatment are given in parentheses."

That healing finally occurs in many cases and is demonstrable by X-ray is demonstrated by our cases where control examination was made six months or more after beginning treatment. This is in accord with the findings of Buckstein (2), who reported disappearance of the *niche* after treatment in three cases with corresponding relief of symptoms. In his cases, too, this was shown six months or more after the first examination. The same is true of the second case reported by Clark and Geyman (1).

That we call attention to these facts seems justified because the question of demonstrating activity of duodenal ulcer by means of X-ray is not as yet a settled problem. Thus Clark and Geyman come to the almost opposite conclusion that very often it is impossible to still demonstrate evidence of a *niche* on control examination while symptoms persist. They think this is due to the anatomical changes during healing. We, however, would be inclined to credit this persistence of symptoms to another cause. Though we agree that for some cases their explanation may be valid or that certain technical factors may be disturbing in visualizing the *niche* we think another factor must be considered, namely, gastritis, which practically always accompanies ulcer. We often found gastritis with a healed ulcer. It is beyond the scope of this paper to discuss this in detail, as it would involve the whole question of etiology of peptic ulcer and also the question of X-ray diagnosis of gastritis. Where deformity of the duodenal cap alone is the basis of diagnosis, no information can be obtained concerning the activity of the ulcer. This has been shown by the work of Emory and Monroe (12).

Although we are fully aware of the pitfalls to which even compression technique is liable in demonstrating the presence or absence of a niche, we do not agree with the opinion that the determination of activity should be left to the clinician alone. We feel justified in emphasizing that the roentgenologist can play a valuable part in determining the degree of activity. In duodenal ulcer, visualization of the anatomical lesion can be of definite value not only in making the diagnosis, but also in determining the prognosis and method of treatment.

SUMMARY

1. By means of the compression technique with "aimed exposures," it is possible to demonstrate the *niche* in a large percentage of duodenal ulcers.

2. Control examinations where the *niche* has been demonstrated are of great value in determining activity or progress in healing while under treatment.

3. A large percentage of cases shows persistence of the *niche* for a considerable period of time after symptoms are clinically relieved.

4. After a sufficiently long period has elapsed, complete healing may be demonstrated in these cases by X-ray.

5. Localization of the ulcer is of value in the prognosis of complications.

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ABSTRACTS

FRIK, O. H.

Tumors of the Stomach and Alimentary Canal Which Are Difficult to Visualize in the X-ray and Their Different Diagnostic Interpretations. Fortsch. auf dem Gebiete der Roentgen Strahlen, May, 1934.

Localization of benign or malignant tumors of the stomach wall is best attained by modified compression methods in conjunction with aimed exposures. The usage of small amounts of barium reveals stage of mucous folds therefore displaying a more exact topographical condition. A complete filling may overlap tumors of smaller size. If situated on areas hardly accessible to palpation such filling may make detection of tumors very difficult. Myomata of the stomach show often blood in the stools, very likely due to accompanying gastritis. Smaller polypi are recognizable only with a careful and scanty barium examination employing the above method.

M. E. Gabor (Milwaukee, Wis.).

SECTION V—*Therapeutics*

A NEW TYPE OF SERUM THERAPY FOR THE TREATMENT OF NON-SPECIFIC ULCERATIVE COLITIS*

PRELIMINARY REPORT

By

GREGORY SHWARTZMAN, M.D.

and

ASHER WINKELSTEIN, M.D.

NEW YORK CITY, NEW YORK

STUDIES on the phenomenon of local skin reactivity to bacterial filtrates clearly demonstrated the synergistic effect of micro-organisms. Under experimental conditions, tissues made vulnerable through contact with toxic filtrate of one micro-organism became receptive to the severe injurious effect of toxins of a large group of apparently biologically unrelated micro-organisms (among these *B. coli, B. influenzae,* streptococcus, etc.) (1). These experiments, therefore, bring into prominence the *rôle* of toxins of secondary invaders or normal bacterial inhabitants upon the evolution of diseases resulting from the specific infections.

It is our opinion that the etiology of *non-specific* ulcerative colitis is not established as yet. Nevertheless, whatever the primary, etiological micro-organism may be, tissues rendered vulnerable by it may become receptive to the effect of natural bacterial inhabitants of the body. Among the stool micro-organisms, one particularly worthy of study along these lines is *B. coli.*

The phenomenon of local skin reactivity to *B. coli* made possible the demonstration and the quantitative determination of potent exotoxic, antigenic substances in *B. coli* culture filtrates (2). Horses were immunized by subcutaneous injections of pooled toxins and intravenous injections of vaccines of strains of *B. coli* obtained from normal stools and various pathological conditions. After a period of several months, sera were produced which were capable of neutralizing *B. coli toxin* in multiple proportions. The exact methods for determining the titers of these sera were previously described (3). While primarily intended for the treatment of surgical peritonitis, their use in non-specific colitis was suggested by Winkelstein. Accordingly, a group of 21 patients affected with non-specific colitis was treated with anti-coli, immune horse sera containing from 35 to 75 "phenomenon-neutralizing" units; from 800 to 1,600 agglutinating and from 8 to 16 precipitating units, as follows:

Method: Following a control period of two weeks, during which emetine and symptomatic therapy were given, conjunctival and intradermal sensitivity tests were performed. If negative, 0.5 c.c., 2 c.c. and 5 c.c. were administered intramuscularly at six-hour intervals during the first day. If these injections were not followed by severe reactions (chills, fever, urticaria), intravenous medication was given during the next 48 hours. It seems important to give large quantities of the serum in a short space of time, otherwise the antitoxin leaves the blood stream quickly (4). However, because of the possibility of dangerous shock, despite negative sensitivity tests, the following precautions were observed: (1) adrenalin solution was administered even for slight reactions; (2) divided dosage was employed—from 25 c.c. to 100 c.c.—until 300 c.c. were given; (3) when the dose exceeded 25 c.c., the drip-method consuming at least one hour was used. In this group chills and moderate rises in temperature were encountered only twice. Urticaria (mild to severe) was the rule in from 2 to 19 days after exhibition of the serum therapy. In three cases (two children and one adult), the serum was administered intramuscularly.

Material: During the past year, 21 cases of non-specific colitis have been treated. Sixteen were septic cases. All had long-standing, severe colitis, associated with badly ulcerated mucous membranes and bloody, purulent diarrhea. Bacillary dysentery was excluded bacteriologically and serologically. Amoebae were not encountered and all patients underwent the therapeutic test with emetine without improvement.

Outcome: In 18 of the 21 cases treated, the results were good. In fact, in 15 cases the improvement was striking as evidenced by abrupt drop in temperature, reduced number of stools, and clinical well-being of the patients within from two to six days. In these patients, the stools became formed and, sigmoidoscopically, the ulcerations had disappeared in from two to three weeks. In three other cases the improvement was noted in one to three weeks. The remaining three cases were considered therapeutic failures. One of these three failures developed a peri-sigmoid abscess, even though the mucosal ulcers healed. In another case, the serum was administered very early—on the tenth day of a very septic course. A study of the toxin of this patient's *B. coli* revealed an absence of neutralization by the serum used. Ten cases have been followed for from six months to one year. Two of this

group experienced mild recurrences—one at seven months and one a year after treatment.

Discussion: In this hospital polyvalent, anti-dysentery horse serum and Bargen's concentrated serum have been administered repeatedly to patients with non-specific ulcerative colitis. We have not been impressed favorably by the results. However, inasmuch as equivalent amounts of sera were not used, this series is not considered a proper control to the series with anti-coli serum. An adequate control experiment is under way.

A complete consideration of these cases and the therapy employed will not be given in this brief report. No claim is made for the etiologic *rôle* of the *B. coli* in this disease. It may be a factor of significance as a primary or secondary invader, or it may not participate in causing or maintaining the affection. The therapeutic results obtained may have been due to a non-specific influence of the large amount of horse serum administered within a short period of time. We are led to present a preliminary report of the results with this serum now because (1) its use seems logical, (2) the results in this fairly large group of seriously ill patients appear unusually satisfactory, (3) the method of treatment offers a new line of investigation and therapy of a disabling and baffling malady, and (4) since the non-specific, protein reactions (chills and elevations of temperature) were observed only in a few instances, apparently they were not responsible for the amelioration of the ailment.

It seems necessary to prepare a serum in which are employed pooled strains of *B. coli* from patients affected with severe ulcerative colitis. Possibly concentrated sera will give even better results. Should therapeusis with the exhibition of such concentrated sera prove successful, a study of the *rôle* of multiple strains of *B. coli* in the etiology of the disease then should be made.

SUMMARY

1. There is described a method of treatment of *non-specific*, ulcerative colitis in which is employed antitoxic, anti-coli horse serum of a high neutralizing titer, as determined by means of the phenomenon of local skin reactivity to *B. coli*.

2. In 21 cases so treated, the clinical results were good in 18 instances; failure was encountered in three patients.

3. The preparation of an improved concentrated serum is suggested; further studies upon the significance of various strains of *B. coli* (etiologically and therapeutically), with respect to non-specific ulcerative colitis would appear to offer a fruitful field of investigation.

The work was aided by a grant from the Altman Foundation for which grateful acknowledgments are made.

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ABSTRACTS

ANDERSON, HAMILTON H., AND REED, ALFRED C.

Carbarsone Rectally in Amebiasis. Amer. Jour. Trop. Med., 14:257-269, 1934.

Following a cleansing enema, 200 c.c. of a 2 per cent sodium bicarbonate solution, containing 1 per cent carbarsone, was instilled into the rectum to be retained over night. Each case received 5 such treatments, amounting to the administration of 10 grams of carbarsone. Dysenteric symptoms were relieved by using carbarsone rectally, but the amebae were not eradicated completely, thus requiring the drug to be given orally. Some cases received either emetine, bismuth subcarbonate or vioform instead of carbarsone orally. The authors feel that the rectal administration of carbarsone offers another method of treatment in refractory cases.

W. C. Boeck.

ANDERSON, HAMILTON H., AND REED, ALFRED C.

Untoward Effects of Anti-Amebic Drugs. Amer. Jour. Trop. Med., 14:269-282, 1934.

A report of individual cases in which certain untoward clinical effects are attributed to the use of emetine, acetarsone (stovarsol), cheniofon ("yatren" or "anayodin"), vioform, dihydranol, and bismuth subnitrate, in the treatment of amebic infection. Carbarsone was given to 330 patients without any untoward effects except in one case with an associated hepatitis. In the one case cited in which emetine was given, vomiting occurred throughout the course of a total 12 grains given subcutaneously, and was followed by an apparent cure, but also by a complaint of weakness, pain in the legs, loss of energy, breathlessness on exertion, palpitation, and vertigo. These latter effects still continued 15 months after treatment, and an electrocardiographic study revealed a partial A-V block (Q.R.S. 0.12). A year later, another tracing showed a similar finding and, in the opinion of the authors, this evidence of myocardial damage was due to the emetine treatment of two years before. (However, this conclusion must be only speculative, since no tracing was taken before the time of the emetine treatment to reveal the electrocardiographic status of the heart. Abstracter).

W. C. Boeck.

GUIDO, FRANK R.

A Rational, Non-surgical Treatment for Intestinal Fistulas —Report of a Case. J. A. M. A., 102:2176, June 30, 1934.

From both clinical and experimental observation it is clear that the leak from intestinal fistulas must be controlled and stopped for, in the first place, the loss of intestinal juices which are so essential to the body must be prevented and, secondly, digestion of the abdominal wall with the resultant slough and infection must be prevented. The author places emphasis on a form of non-operative therapy to be used in closing up these fistulas. The procedure is simple, physiologically rational and attended with excellent results. It was suggested originally by Potter that the application of tenth-normal hydrochloric acid would tend to neutralize the alkalinity of the wound discharge and thus aid healing. Guido employed this agent in the case of a fistula of the ileum with remarkable success. This fistula had shown no signs of closing spontaneously.

Samuel Morrison.

SECTION VI—*Abdominal Surgery*

CARCINOMA OF THE COLON

By

ROSCOE R. GRAHAM, M.B.*
TORONTO, CANADA

CARCINOMA of the colon is a very lethal disease. The anatomical arrangement of the colon lends itself to thorough, wide and radical extirpation. We would suggest that this terrific mortality accompanying this disease is due to two factors—first, failure to diagnose the lesion at a time when it may be completely extirpated by a surgical procedure, and second, the lack of appreciation of the fact that the immediate cause of death in many instances is intestinal obstruction. Many of these patients are operated upon for cancer when they really should be operated upon for intestinal obstruction.

The observations which we present are based upon the analysis of 116 cases of carcinoma of the colon and 105 cases of acute intestinal obstruction. The distribution of the carcinoma of the colon is illustrated in Table 1.

TABLE I

Caecum	12
Ascending Colon	11
Transverse Colon	12
Descending Colon	8
Sigmoid	33
Rectum	40

The ratio of lesions of the colon to those of the small bowel in producing *acute* intestinal obstruction is illustrated by an analysis of 105 consecutive cases of *acute* obstruction, as indicated in Table 2.

TABLE II

Total number of Cases	104
Small Bowel Lesions	80—77%
Large Bowel Lesions	24—23%
(a) Carcinoma	19—79%
(b) Volvulus of Caecum	1— 4%
(c) Sigmoid	1— 4%
Bands about the Colon	3—13%

Eighteen per cent of all instances of Acute Intestinal Obstruction are due to Carcinoma of the Colon.

These figures should impress one with two facts: First—in adults suffering from acute intestinal obstruction, carcinoma of the colon must be considered as one of the possible causes. In this series it was the etiological factor in 18 per cent of instances. The second point which is worthy of note is in acute intestinal obstruction, the obstructive factor is in the large bowel in 23 per cent of instances. When the seat of the obstructing lesion is definitely localized in the colon, 75 per cent of these cases will be due to carcinoma.

The *site of the carcinoma* which will produce an acute obstruction is interesting. In our cases, all the obstructing carcinomas were situated in the left large bowel, that is from just proximal to the splenic flexure, to the rectum. Burgess, of Manchester, reports 87 per cent in the left large bowel and 13 per cent proximal to this. It is important, however, to realize, first, that there are carcinomata involving the colon which do not produce obstruction, and second, that invariably patients who suffer an acute obstruction due to cancer of the colon had previously suffered for a varying length of time from chronic obstruction of the colon. Whether the malignant lesion in the colon will produce obstruction or not is dependent upon the nature of the lesion.

We have recognized two main types of gross lesions representing carcinoma of the colon—first, and by far the commoner, the small constricting annular carcinoma; and second, the large, fungating carcinoma involving only a portion of the circumference. In our experience this latter type is found but rarely, apart from the caecum and rectum. Such a lesion is characterized by bleeding, either massive or occult. This leads to the observation that any patient who is suffering severe, unexplained secondary anaemia should be suspected of harboring a carcinoma of the colon until this diagnosis is disproven. The patient showing *blood in the stool*, in the absence of haemorrhoids or any lesion visible in the rectum or lower sigmoid with the sigmoidoscope, and who is proven not to be suffering from gastric or duodenal ulceration or malignancy, is probably harboring a carcinoma of the caecum. The source of haemorrhage, if it be due to carcinoma of the rectum, may readily be determined by digital or proctoscopic examination of the rectum.

To diagnose, however, a *chronic obstruction* due to carcinoma of the colon, one must be very alert and recognize the most subtle departures from normal in large bowel function. The basic factor in making one suspect the diagnosis of a stenosing carcinoma of the colon is the principle of *suspecting every patient past forty years of age who for the first time begins to suffer from increasing constipation.* The exception to this aphorism is occasionally found in patients who harbor a carcinoma of the caecum. Having previously suffered from constipation, the irritation of an early caecal carcinoma may produce a daily stool. An increasing girth and a descreasing weight is highly suggestive. Chronic obstruction of the large bowel differs from a similar phenomenon in the small bowel by the absence of vomiting and crampy pains. One may find at operation irrefutable evidence of a high degree of

*Assistant Professor of Surgery, University of Toronto; Senior Surgeon, The Toronto General Hospital.
Submitted August 2, 1934.

obstruction, and the patient never admitting any crampy pain or vomiting, but if we inquire carefully into his previous history, he will have suffered from attacks of acute abdominal pain of varying intensity and duration, which were only relieved by the administration of very drastic cathartics and repeated enemata.

Given a patient with this history, it is highly disastrous if he should, without further investigation, come under the treatment of a competent internist, because proper selection of diet, and therapy directed towards the treatment of the common idiopathic constipation, will help even those patients in whom the constipation is due to carcinoma of the colon, and valuable time may be lost before the diagnosis becomes sufficiently established to warrant operation.

The site of the carcinoma also determines to a degree the symptomatology. (Figure 1.) In carcinoma

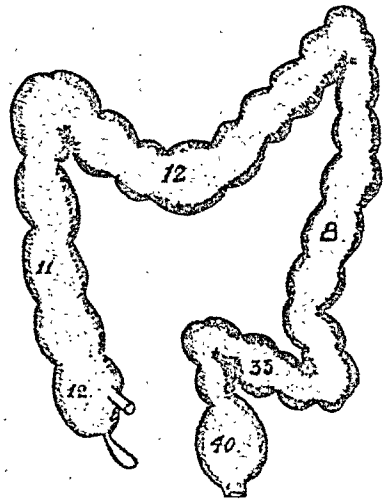


Fig. 1. Schematic outline of the Colon showing the incidence of carcinoma in each area.

of the caecum, the formation of an abscess in the right iliac fossa due to the perforation of a fungating carcinoma on the posterior wall of the caecum is often the first evidence of disease which compels the patient to consult the physician. In the eleven cases of carcinoma involving the ascending colon, all showed definite clinical evidence of obstruction, seven showing sub-acute obstruction longer than one week. Eight of the eleven cases had a definite history of increasing constipation. Only one case had a history of passing blood and mucus, and only three had diarrhoea. In the twelve cases involving the transverse colon, chronic obstruction was present in seven, four of which were definitely acute. Ten had a history of increasing constipation, and two only a history of passing blood and mucus. None had diarrhoea. In the eight cases involving the descending colon, all had a history of increasing constipation, and five were admitted with acute obstruction. None of these cases had diarrhoea. Of the thirty-three cases of carcinoma of the sigmoid, seventeen, or 50 per cent, were admitted with acute intestinal obstruction. Twelve per cent previously had been operated upon for haemorrhoids. The average duration of symptoms for which the patient sought relief was nine and a half months, and varied from three weeks to two years.

In this group of thirty-three cases, twenty-two were operable for cure as far as the carcinomatous involvement was concerned, but in the cases suffering from acute intestinal obstruction there were nine deaths. It is of great significance to realize that these deaths were due not to carcinoma, but to intestinal obstruction.

In the forty cases of carcinoma of the rectum, it was possible to resect twenty-seven, or 66 per cent. Ten per cent previously had been operated upon for haemorrhoids. Gross bleeding was present in 32.5 per cent and tenesmus was present in 42.5 per cent.

With this data before us it becomes obvious that if we took seriously a history of increasing constipation plus a digital examination of the rectum as indicative of large bowel carcinoma, the percentage of late cases which would present themselves for treatment would be very appreciably diminished. (Figure 2—Mr. A.)



Fig. 2. A Barium Enema, showing Carcinoma in the Rectal Ampulla, which should have been diagnosed by digital examination, making Barium Enema unnecessary.

It is important in the investigation of such patients to realize that negative information following X-ray examination with a barium enema is no assurance whatever that the patient may not be suffering from a carcinoma of the colon. This is no reflection on the method of examination, nor on the radiologist, but a recognition of the limitations of absolute accuracy of this procedure is most important. The use of the sigmoidoscope never should be omitted in the investigation of such patients.

In a previous analysis of cases of this disease in which the patients were admitted suffering from acute intestinal obstruction, it was forcibly impressed upon us that a great contributing factor in our mortality was the *type* of operative procedure which was carried out. One is so impressed with the fact that the patient is suffering from a carcinoma which if left *in situ* will be inevitably fatal, that we have been prone to overlook the physiological disturbance produced by the obstruction. This latter phenomenon really is the basic lesion which brought these people to the hospital. We enunciated, therefore, the principle that *if a patient is admitted to hospital suffering from acute intestinal obstruction due to a carcinoma of the colon, he should be operated upon for intestinal obstruction and not for cancer.* What does this mean? We interpret it as indicating a surgical procedure as minor as may be compatible with the relief of the obstruction, without any effort whatever being directed at the moment towards the treatment of the carcinoma. Previously we

had in cases of acute intestinal obstruction opened the abdomen, proven the diagnosis and the presence or absence of secondaries, and then done either a colostomy or a Mickulicz type of extirpation. This method of dealing with acute intestinal obstruction due to carcinoma of the colon resulted, in our hands, in the staggering mortality of 68 per cent.

Our *incidence of large bowel obstruction* has been similar to that of other observers. Soutar in a four-year period, 1920 to 1924, reports 43.5 per cent of carcinoma of the colon dying of obstruction. Burgess, of Manchester, had 35.6 per cent of his cases of carcinoma of the colon admitted with complete obstruction. Haggard (1) had 90 per cent of instances of intestinal obstruction of the large bowel due to cancer, compared with our 79.1 per cent. The mortality following acute obstruction of the colon due to cancer in other hands leaves much to be desired. The performance of a left iliac colostomy to relieve acute intestinal obstruction as reported from the Brigham Hospital in Boston gave 39.1 per cent mortality. Gray Turner, Newcastle-on-Tyne, 39 per cent; Mayo Clinic, 42.85 per cent. When one considers that the mortality following a palliative colostomy for an inoperable carcinoma in the absence of an acute obstruction is only 7.67 per cent in our series, there surely can be no more forceful presentation to show the tremendous factor which the obstruction plays in the primary mortality. As a result of this, we have now changed our method of handling these cases. When a patient is admitted who is suspected of suffering from a large bowel obstruction, a flat X-ray plate is taken. (Figure 3—Mrs. S.) This

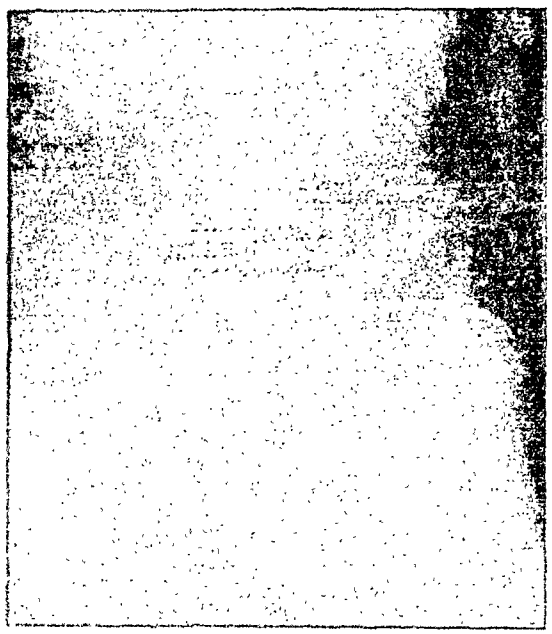


Fig. 3. Acute Intestinal Obstruction, showing dilated coils of Large Bowel.

will show very well the distention of the caecum, but in order to be certain that the gas shadow of the caecum is not misinterpreted, a barium enema is given, and the sharp delimitation of its course marks the site of the carcinoma. (Figure 4—Mrs. S.)

Drainage of the gastro-intestinal tract proximal to the obstructing lesion is sufficient to save the patient from death due to intestinal obstruction. This we feel can be accomplished safely and simply by means of a blind caecostomy. We have had sixteen cases of acute

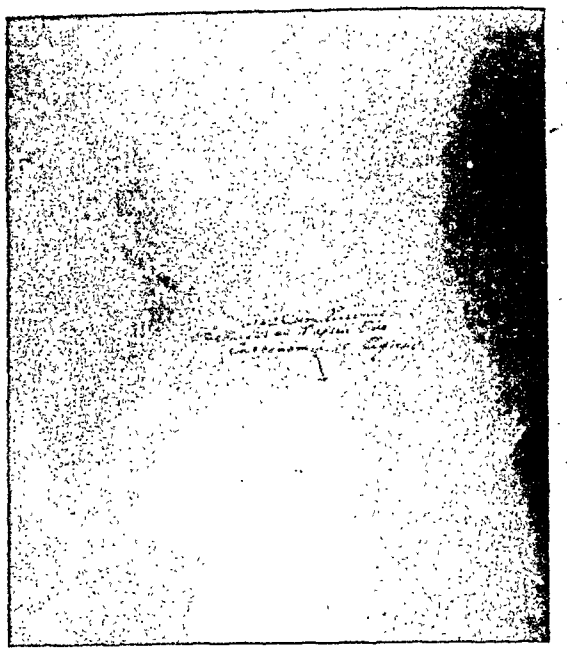


Fig. 4. Same case as "Fig. 3", showing the localization of the obstruction by Barium Enema.

intestinal obstruction due to cancer of the colon in which we have done a blind caecostomy with two deaths. In one obstruction was present for a week and the caecum had patches of gangrene. The second case died of inanition from a carcinoma of the transverse colon penetrating retro-peritoneal tissues. This tremendous decrease over our previous mortality, and the marked decrease as compared with the reported mortality by competent surgeons following the making of a colostomy in such circumstances, commends itself to us as a safe and sound procedure. If, after the patient recovers from the acute obstruction, it is found that the site of the carcinoma is so low in the left colon as to demand a permanent colostomy, we may, at the second operation, do only a left iliac colostomy. We have found in the low growth that even at the end of three weeks there is still considerable oedema and dilatation of the sigmoid. Failure to observe this principle we charge as the cause of death in one of our patients, due to peritonitis following an abdomino-perineal excison of a recto-sigmoid carcinoma. We have come to recognize the fact that any undue manipulation of a distended, oedematous colon is disastrous, and too often is followed by peritonitis.

In operating upon patients who have given a history of chronic obstruction, if the lesion be situated to the left of the middle of the transverse colon and proximal to the recto-sigmoid, we always do a two-stage operation, the preliminary procedure being a blind caecostomy. (Figure 5—H. McI.) This permits of irrigation of the colon and allows the oedema in the wall to subside. This latter factor we believe is of tremendous importance in preventing the spread of infection at the second operation, because, as Rankin has shown, the peri-colon areolar tissue, in the presence of obstruction and oedema, contains organisms capable of recovery by culture. Further, the technical difficulty of an anastomosis in a non-oedematous bowel is much less and much safer than it is if one attempts a similar procedure in a thickened, oedematous bowel wall. If the lesion be so situated that a permanent colostomy is demanded for thorough eradication of the disease, we believe that a two-stage operation is preferable to

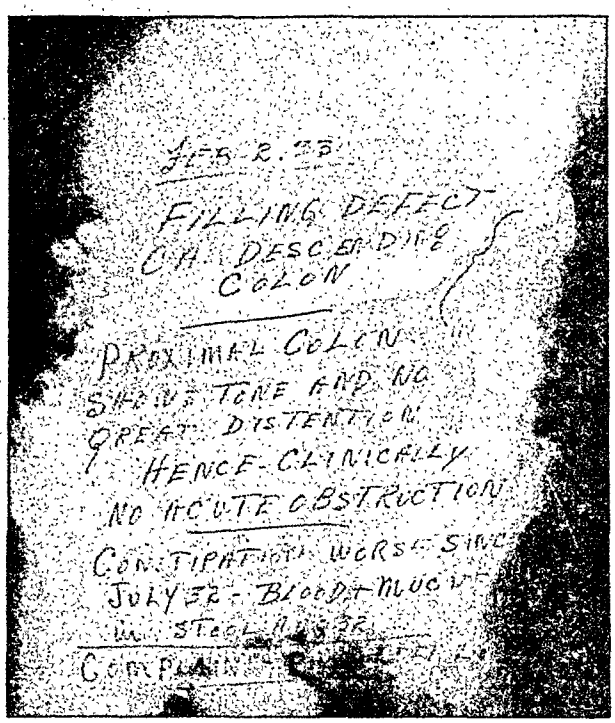


Fig. 5. Barium Enema outlining a defect in the Descending Colon without Acute Obstruction.

a single-stage procedure, if there is the slightest evidence of obstruction.

The site of a carcinoma requiring permanent colostomy is from the recto-sigmoid junction to anal orifice. We know of no way in which the wall of the bowel can be restored to normal more effectively than by the doing of a colostomy. Irrigation of the proximal and distal colon is carried out daily and the lower bowel to be excised can be rendered almost sterile. With growths in this latter site we must debate the wisdom of choosing between the abdomino-perineal and the perineal method of excision. Ardent advocates of the abdomino-perineal operation find no place for solely a perineal excision. Were it possible to do an abdomino-perineal excision with as low a mortality as one can do a perineal excision, there would be no argument, but in our hands an abdomino-perineal excision of the rectum carried with it a higher mortality than did the perineal excision. Further, we have, in many instances, completely extirpated the growth by means of a perineal excision, if one can use freedom of lymphatic metastases as an index of thorough eradication.

We are taking the attitude at the moment that if the carcinoma of the rectum is readily palpable on digital examination, there must be very good reason why the abdomino-perineal excision should be chosen in preference to the perineal excision. If the carcinoma is situated *proximal* to the middle of the transverse colon, we remove the lesion in one operation, in the absence of acute obstruction. The reason for this lies in the physiological function of the colon. (Figure 6.) Ninety per cent of the fluids and 10 per cent of the solids in the gastro-intestinal tract are absorbed in the area from the caecum to the splenic flexure, which means that the content of the right colon is fluid or semi-solid, whereas the content of the left colon is invariably more solid. Therefore, if we are pouring fluid instead of solid or semi-solid contents through the anastomosis, the likelihood of obstruction developing at the site of the anastomosis is much less. We do an end-to-end suture of the terminal ileum to distal transverse colon over a rubber tube, as suggested by the late Dr. F. N. G. Starr. This procedure has given us most uniformly happy results, and our mortality in resection of the right large bowel now does not exceed the mortality of any other major abdominal operation, whereas our mortality in resection of the left large bowel, including rectum, carries with it a mortality of approximately 10 per cent. This we believe to be due to the mechanical difficulty of passing desiccated bowel content through the anastomosis in the left large bowel. Recently we have tried to overcome this in lesions of the proximal sigmoid and descending colon by a resection extending from the middle of the transverse colon to the distal third of the sigmoid, restoration being accomplished by an end-to-end suture, the presence of the caecostomy being a safety-valve, and preventing increased strain being placed on the newly-made anastomosis. The original use of a caecostomy in this disease, as suggested by Sir Harold Stiles (2), consisted in fastening a tube into the caecum after the Witzel method. This has not yielded happy results in our hands, and we now bring out a portion of the caecum one inch in diameter through a small McBurney incision. Four interrupted sutures only are placed between the wall of the caecum and the skin. Failure to suture the caecum to the skin results in a retraction of the caecum into the peritoneal cavity, and materially decreases, if not in many instances nullifying its usefulness. It is opened by a cautery in from twelve to forty-eight hours, depending upon the severity of the obstruction. In the meantime, the patient is supported by the administration of many thousand c.c.'s of saline, intravenously. Even though the patient be suffering from acute intestinal obstruction, it is surprising how the correction of the dehydration safely permits a delay of from twelve to forty-eight hours in opening the caecostomy. We then instill six ounces of raw linseed oil into the caecum every four hours, until it appears per rectum. Its appearance per rectum coincides with the subsidence of the oedema at the site of the obstructing carcinoma. This is then followed by daily saline irrigations, both through the caecostomy and per rectum. In this way the subsidence of the oedema in the bowel wall is hastened, and all scybala are removed from the colon. The patients are allowed to be out of bed at the end of a week or ten days, and the second stage operation is not undertaken until two and a half to three weeks following the making of the caecostomy. In this way patients have entirely recovered from the physiological disturbance attendant upon their obstruction, and one may then, with great safety, deal directly with the carcinoma. Following

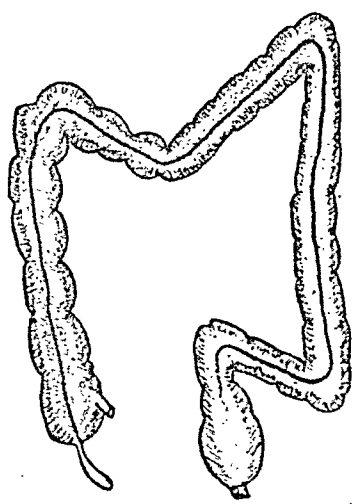


Fig. 6. Schematic drawing of the Colon, the shaded area being the safety zone in the Colon, in which the content is fluid, and single-stage operations may be undertaken.

resection of the carcinoma, be it proximal to the recto-sigmoid, in which by choice reconstruction is done by means of an end-to-end anastomosis, raw linseed oil again is introduced through the caecostomy in order to maintain the fluid content of the colon proximal to the anastomosis. The escape of gas and small bowel content through the caecostomy prevents undue strain being placed on the suture line. This method of procedure has in our hands resulted most happily in dealing with this difficult problem. This type of caecostomy will not close spontaneously, and we have chosen to defer closing the caecostomy until three months following the resection of the growth. In this way the anastomosis has become firm, all oedema has disappeared both about the caecostomy and the anastomosis, and the amount of leak from the caecostomy when the obstruction has been relieved is very slight. In our experience the operative wound in closing the caecostomy at this time invariably heals *per primum*. These advantages we feel outweigh any inconvenience which the prolonged convalescence may entail.

CONCLUSIONS

(1) Association of intestinal obstruction with carcinoma of the colon is the most important factor contributing to the immediate mortality of this disease.

(2) The diagnosis of chronic intestinal obstruction can only be made after carefully-taken clinical history, properly interpreted. It is very important to recognize subtle departures from normal function of the colon.

(3) Any patient past forty years of age who for the first time in his life suffers from an increasing constipation must be considered to be suffering from carcinoma of the colon until this is disproved.

(4) A negative finding following X-ray examination with a barium enema is no assurance that the patient is not suffering from carcinoma of the colon.

(5) Operation undertaken on patients suffering from acute intestinal obstruction due to carcinoma of the colon should be the most minor procedure compatible with relief of the obstruction.

(6) We should not operate on a patient for cancer when he is suffering from an intestinal obstruction.

(7) A blind caecostomy is the ideal procedure for the relief of obstruction due to cancer of the colon.

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ABSTRACTS

JOHNSTON, LLOYD B., AND RENNER, GEORGE, JR.

Peptic Ulcer of Meckel's Diverticulum. A Report of Two Cases and a Review of the Literature. S. G. and O., 59: 198-209.

The authors deserve much credit for condensing so much valuable information regarding peptic ulcer of Meckel's diverticulum. In tabulated form, they give the essential findings in all 76 cases previously reported in the literature and add two cases of their own. The bibliography is most complete.

Ulcer associated with Meckel's diverticulum was found to be more common in male infants and in children. It was usually single and resembled the marginal ulcer at a gastro-enterostomy stoma, in that it was generally located at the base of the diverticulum at the junction of the gastric and ileal mucosa.

Intestinal hemorrhage, usually massive, was the most constant sign. If recovery occurs without operation there is likely to be a recurrence. In several cases, in older children and adults, some abdominal distress has been noted. Perforation occurs in over 50 per cent of the cases.

In the Meckel ulcer, colic-like distress at the onset of a hemorrhage can be differentiated from that of intussusception in that it is less acute and of shorter duration. Walled-off perforations present variable degrees of tenderness, rigidity and distention but a palpable mass seldom can be demonstrated. This group of cases is most likely to be confused with appendicitis, appendiceal abscess of intussusception. An acute perforation with diffuse peritonitis gives the usual picture of an "acute surgical abdomen". Blood dyscrasias are eliminated by the laboratory studies demonstrating normal bleeding and clotting time; gastric and duodenal ulcers by negative X-ray findings and absence of digestive symptoms; rectal polypi by palpation or proctoscopic examination, and intussusception by the lack of obstructive signs, the previously mentioned lack of intense colic, the absence of palpable mass, and the absence of mucus in the stool. Other and rarer conditions may be accompanied by intestinal bleeding but seldom by massive hemorrhage.

The treatment essentially is surgical. Cases with hemorrhage should be transfused one or more times as indicated and then explored. Apparent improvement should not lead to postponement of operation since recurrence is the rule. Perforation may occur during the time the patient is being prepared so as to be a better operative risk. If it does, then or without previous hemorrhage, immediate laparotomy is indicated. Excision of the diverticulum is the usual treatment but resection of a segment of bowel may be required in some instances.

The mortality record is excellent except in those cases associated with general peritonitis, then it is more than 50 per cent; however, patients not treated surgically exhibit a mortality of nearly 100 per cent.

J. Duffy Hancock (Louisville, Ky.).

BRANDSON, B. J.

The Early Diagnosis of Cancer of the Intestine. Can. Med. Jour., June, 1934, p. 630.

Treatment of cancer, surgical or by radiation, must be early to be successful. The prognosis in cancer of the bowel is more favorable than in any other organ. The most important early symptom is a change in bowel habit, and the next is the presence of blood in the stool. Pain is not often an early symptom, and weakness, anemia and loss of weight are earlier and more common symptoms in cancer of the stomach. A digital examination of the rectum should always be made before the proctoscope or sigmoidoscope is used, and when disease is in the rectum the diagnosis can be accurately made by this means alone. If the digital examination is negative, the proctoscope should then be used. If the instrumental examination is also negative, an X-ray examination should be made. A barium enema is preferable to giving barium by mouth because of the danger of causing obstruction. In considering the differential diagnosis, diverticulosis of the sigmoid, hyperplastic tuberculosis of the caecum must be considered, and a retrocaecal appendix may be mistaken for a new growth.

R. H. M. Hardisty.

GRAHAM, ROSCOE R.

Cancer of the Stomach. Can. Med. Jour., April, 1934, p. 398.

The affection occurs in 3 per cent of all complaining of gastro-intestinal symptoms, and we must be eternally on the watch for it. The only cure is surgery; 50 per cent of cases are inoperable when seen.

Resection is advised more frequently than formerly; if no cure a longer life and more comfort are assured.

Where obstruction, gastroenterostomy gives only a very short freedom from symptoms, and where no obstruction it is useless.

Instead of looking for symptoms and signs, the author thinks a patient over forty who for the first time suffers from *continuous indigestion* should be suspected of having a gastric carcinoma till disproved.

He thinks a valuable procedure is gastric analysis, and the determination or not of free hydrochloric acid, for though carcinoma may occur with free HCl, it is very uncommon. If no free HCl pernicious anemia and chronic cholecystitis must be ruled out; absence of HCl also occurs in a certain number of normal persons, but if present he quotes Hurst, as saying, the

patient will have no cancer of stomach for at least five years.

He emphasizes the fact that X-rays are not infallible and that even the most experienced surgeons cannot always be certain that a lesion is malignant—not even when the abdomen is opened. He states re-examination of labeled museum specimens "benign gastric ulcer" showed malignancy in 18 p.c. Pyloric lesions are much more frequently malignant than benign and in his experience benign pyloric ulcer does not cause stenosis.

When a patient with a stenosing pyloric lesion is to be operated upon the value of preoperative fluid, diet and lavage and washing after operation is emphasized. By these means existing oedema of the stomach wall is lessened and also the danger of peritonitis.

By these measures, the patient is given the best possible chance of cure or a longer, more comfortable existence.

R. H. M. Hardisty.

PRIESTLEY, JAMES J., AND WALTERS, WALTMAN.

Indications for Operation in Gastric Syphilis. S., G. and O. 58:1030-1035, June, 1934.

The diagnosis of gastric syphilis is often difficult, probably because of the rarity of the condition (gastric syphilis occurring three times in a thousand cases of syphilis). It is however important since the treatment of it is so different from that of gastric carcinoma from which it has most often to be differentiated.

Points of diagnostic importance are the usual incidence in the second to the fourth decade of life, the marked and progressive gastric symptoms of an average duration of two years, and the usual absence of an epigastric mass, retention, nausea, anemia, cachexia and bleeding. The most frequent gastric complaints are inability to eat a full meal, epigastric soreness, and bloating and belching after eating. The X-ray findings may vary but usually the site of the lesion shows a tubular segment with a smooth lumen, "stiffening, lessened mobility, and absence of peristalsis".

Patients presenting gastric lesions with positive serological evidence of syphilis are classified into one of three main groups for the determination of the proper method of treatment: (1) cases which appear to present a rather definite picture of gastric syphilis and cases which rather definitely present inoperable gastric lesions are primarily medical; (2) cases where there is an incidental syphilis associated with an operable gastric malignancy or non-specific inflammatory gastric lesion requiring operation; and (3) cases presenting positive evidence of syphilis and a definite gastric lesion indeterminate in diagnosis between syphilis and malignancy. Cases in groups (2) and (3) generally require exploration alone or occasionally combined with preliminary medical treatment. The combined treatment would seem to apply particularly to those in group (3).

Purely syphilitic gastric lesions usually show a spectacular response (79 per cent) to antisyphilitic treatment. Definite improvement is usually noticeable in 2 or 3 weeks but 4 or 6 weeks may elapse before appreciable change occurs. The improvement which rarely occurs following the use of arsenicals in cases of carcinoma is symptomatic rather than anatomical, and is most temporary.

Surgical procedures adopted at time of exploration will be the usual ones for the type of lesion found to be present. The liver and other organs may present such evidence of lues that nothing further than an exploration will be indicated.

Interesting comments by Dr. Paul A. O'Leary and Dr. Geo. B. Eusterman conclude the article.

J. Duffy Hancock.

ROTHENBERG, ROBERT E., AND LINDER, WILLIAM.

"The Single Pyogenic Liver Abscess—A Study of Twenty-four Cases." S., G. and O., 59:31-40, July, 1934.

The importance of differentiating this condition from multiple abscesses of the liver is due to the fact that the treatment is purely surgical and is much more effective than in the cases of multiple abscesses. Single abscesses occur five times more frequently in the right lobe than in the left and usually point to the dome of the liver. While liver infection may occur by way of the portal vein, by way of the hepatic artery, through the bile ducts, by direct extension, by way of the hepatic veins, and through the lymph stream, most of the single abscesses arise through haematogenous infection by the hepatic artery, are of unknown or doubtful etiology, and the pathogenesis strongly resembles that of carbuncle of the kidney and osteomyelitis. On the other hand multiple abscesses are usually of known etiology, arise through the portal veins or bile ducts, and show pylephlebitis or portal vein thrombosis.

The diagnosis of liver abscess may require some days' observation. While the condition may be confused with many possibilities the following rather characteristic syndrome can usually be noted. During the first week or two there were indefinite complaints of malaise and asthenia, a rather rapid loss of weight and strength, fever, occasional chills and some pain in the lower right thoracic region. The fever varied from 99 or 100° F. to 103 or 104° F. Chills, when present, did not have the periodicity noted in multiple abscesses. The pain was usually constant, dull rather than sharp, bore no relation to food intake, and there was inspiratory pain in 39 per cent of the cases. In 82 per cent of the cases the pain was located over the liver area, in 29 per cent it was in the loin and intercostal pain was frequent. Radiation of the pain was rare. Loss of appetite was common but nausea and vomiting unusual. The liver was usually enlarged and tenderness present over liver area—especially significant was intercostal tenderness elicited by deep palpation with one finger. Leucocytosis averaged about 16,000 with polymorphonuclears 86 per cent. There were no characteristic findings in the urine, the presence of bile depending upon the presence of jaundice which was found in only two of the 24 cases, although most patients did have a "muddy" complexion. None of the cases presented ascites.

All of the patients were operated, 58.3 per cent recovering. It was observed that abscess of the dome of the liver approached by a transpleural diaphragmatic two-stage procedure, gave a better prognosis than abscess elsewhere in the liver approached through an abdominal route.

J. Duffy Hancock.

COLLER, FREDERICK A.

"Water Balance in Surgery Patients." S., G. and O., 59: 115-116, July, 1934.

In a rather short but excellent editorial the author directs attention to the maintenance of the proper water balance in surgery patients. He emphasizes the insensible loss of water through the skin which in the average surgical case amounts to 1,000-1,500 cubic centimeters a day but which may be as much as two liters where infection, fever, or hyperthyroidism are factors. In determining the amount of intake needed these two liters must be added to the amount lost by vomiting, diarrhea, and urinary output. The urinary output should be maintained at about 1,500 cubic centimeters a day but it should be borne in mind that low output does not always mean suppression of kidney function. Due to low intake there may not be available enough fluid for the kidneys to utilize. Abnormal losses through diarrhea or inflammatory exudates usually deplete the body fluid electrolytes (sodium and chloride ions) and should be replaced by saline solution. Simple dehydration resulting from limited intake of fluids should be compensated for by 5 per cent glucose solution. Regardless of the fluid given, a happy balance should be maintained—avoiding the dangers of volumes too small and the discomforts of volumes too large.

J. Duffy Hancock.

FREEMAN, NORMAN E., AND BROWN, ROBERT L.

Gastric Lavage in the Treatment of Pyloric Obstruction. S., G. and O., Vol. LVIII, No. 6, pp. 956-959.

The authors observed that in cats with pyloric obstruction those animals whose stomachs were aspirated frequently survived longer than the others. In investigating the factors responsible for the longer survival of certain ones they used healthy adult male, or non-pregnant female cats. The animals had fasted for twenty-four hours and their stomachs were washed clean with distilled water before they were prepared. Under ether anaesthesia, through a mid-line incision, a rubber band one-fourth inch in width was fastened around the pylorus sufficiently securely to cause blanching of the gut. The animals were isolated to avoid psychic stimulation of gastric secretion. They were weighed daily, and rectal temperatures were measured. The vomitus was collected for twenty-four hour periods, though generally there was none until 36 to 48 hours after obstruction. Urine was expressed from the bladder daily in order to avoid contamination of the vomitus. The treated animals had their stomachs emptied and washed out shortly after the operation, and twice daily thereafter. Careful notes about the general condition of the animals were made, and at post-mortem examination the completeness of the obstruction was verified. Six cats served as controls, and five others were subjected to repeated gastric lavage. Determinations were made of the loss of fluids, chloride, protein, and non-protein nitrogen in the gastric contents. Blood chlorides, protein and non-protein nitrogen were estimated before, and three days after the obstruction. These findings were correlated with the loss by way of the stomach and kidneys.

It was found that the animals subjected to gastric lavage twice daily lived almost twice as long as those not so treated. The loss of chlorides and of water was almost twice as great in the untreated animals as in those treated by gastric lavage. The authors conclude that the distention of the stomach causes an increased secretion of fluid and salts into its lumen. The loss of protein by way of the stomach is quite small. They suggest that in clinical cases the benefit derived from gastric lavage is to be attributed to the decrease in the rate of loss of chloride and fluid from the body into the stomach.

Protocols of two animals are given in detail.

Nelson M. Percy.

SCHUTZ, C. B.

Acute Postoperative Obstruction of the Lower Small Intestine. J. A. M. A. 102:1733, May 26, 1934.

The author points out that one of the earliest and perhaps the only specific symptom of the stage of obstruction in the

lower small intestine is uneven distention. He believes that vomiting and obstipation are unreliable criteria on which to base the early diagnosis of low obstruction. If the diagnosis is not established early the presence of generalized distention, the fever, the increased leucocytosis and the decreased or absent peristalsis may be due to peritonitis or obstruction and the differentiation is extremely difficult. In any case the treatment for low intestinal obstruction is essentially the surgical release of the obstructing lesion. Samuel Morrison.

PACK, G. T., AND SCHARNAGEL, I. M.
Gastro-Enterostomy with Exclusion of Inoperable Cancer of Pylorus and Antrum. J. A. M. A. 102:1888, June 2, 1934.

This is a most convincing paper in favor of an operation which apparently is not used frequently enough. The advantages offered by it are enumerated so clearly as to immediately increase its use. Samuel Morrison.

MOERSCH, H. J., AND JUDD, E. STARR.
Diagnosis and Treatment of Pharyngo-Oesophageal Diverticulum: Surgery, Gynecology and Obstetrics. Vol. LVIII. No. 4, April, 1934, pp. 781-786.

Diverticula are divided into traction and pulsion types. Pulsion diverticula are characterized by a pushing out of the mucosa, while traction types are characterized by a dragging out of the wall by adhesions to adjacent glands, or other structures. The pharynx, however, gives rise to two other types of diverticula. The first is of congenital origin arising from bronchial clefts. In such diverticulum the opening of the sac is in the vicinity of the tonsil of pyriform sinus. The second, described by Moynihan, arises between a gap immediately below the border of the cricopharyngeus muscle and the fibers of the esophagus which are descending from their origin at the back of the cricoid cartilage. These have been called lateral diverticula.

Pharyngo-esophageal diverticula are more common among men; ratio of males to females is 4.5 plus to 1. It becomes manifest in later life. The average age of 276 patients with this condition seen at the Mayo clinic was 57.2 years; the youngest 31; the oldest 83. The average duration of pre-operative symptoms was 6.1 years.

The etiology of pulsion diverticula is somewhat obscure. Increased pressure on the pharyngeal wall during swallowing might force the mucosa out through a weakened, or deficient, muscular wall. It has been suggested that negative pressures in deglutition might be of greater importance than positive pressures. Muscular incoordination and spasm of the pharyngeal muscles against a closed esophagus might result in abnormal pressures against the pharyngeal wall. Embryological or developmental anomaly has been suggested as the etiological factor.

The diverticular sac is composed of mucosa and submucosa; rarely are muscle fibers found on it. The sac tends to invade the superior mediastinum; they seldom project below the arch of the aorta. The sac usually lies toward the left side of the neck owing to the anatomical relation of the esophagus to the cervical spine.

The characteristic symptoms are dysphagia, regurgitation, and a typical gurgling noise on eating, speaking or on pressure over the sac when it is distended with air or food. The degree of dysphagia depends on the size of the sac; granular foods are more difficult to swallow than others. Regurgitation occurs when the sac has become large enough to retain liquids and food. It is particularly likely to occur with the patient in the prone position which produces cough. This is a definite risk, for material aspirated during sleep may give rise to pulmonary suppuration. Large pharyngeal diverticulum may produce swelling in the neck, particularly on the left side. It may also cause hoarseness by pressure on the recurrent laryngeal nerve.

The diagnosis may be made from the history. Confirmatory evidence may be obtained by roentgenological examination by esophagoscopy, and by the passage of sounds after the method of Plummer. The presence of stricture with dilatation above it must be kept in mind; carcinoma may be present.

The treatment of pharyngo-esophageal diverticula is primarily surgical. Certain cases may be treated palliatively, particularly elderly patients with small diverticula causing few, if any, symptoms. Palliative treatment pre-operatively must be resorted to when the patient is in such poor condition that immediate operation is inadvisable. The passage of sounds in order to dilate strictures, or to relieve spasm, frequently affords considerable relief. Gastrostomy should be avoided because of the high mortality it carries in elderly emaciated and dehydrated patients. The passage of a Sawyer tube over a previously swallowed silk thread affords an excellent means of feeding.

The authors recommend a two stage operation in which the first stage consists of freeing the sac from the surrounding tissues in the neck and mediastinum, and leaving it prolapsed to the outside of the neck. The wound is closed without drainage. If the sac is too small to reach to the outside of the neck, it is sutured in place, and a silk thread leading to it is brought to the outside of the neck. This facilitates identification of the sac during the second stage. The second stage is done eight days after the first. At this time the sac is loosened from the surrounding tissues by blunt dissection, its neck clamped and the sac cut away. The neck is then sutured over. Recently the trend has been to remove small diverticula in one stage. This can be done safely if the dissection is not carried too far down into the mediastinum.

On a few occasions there has been a tendency toward constriction of the esophagus and some have had fistulae from the esophagus for a while. Dilatation with sounds relieves the stricture. In no case has it been necessary to close the fistulae surgically; sounding has seemed to hasten the healing of those fistulae.

All operative procedures are carried out under local anaesthesia. Nelson M. Percy.

ALLEN, J. H., AND HASKELL, B.
A Two Stage Operation for Fistula-in-Ano. Surgery, Gynecology and Obstetrics. Vol. LVIII, No. 3, March, 1934, pp. 651-654.

The authors describe a two stage operation for large or extensive fistulae in ano. For small superficial fistulae this operation is not recommended.

The procedure is as follows: The internal opening of the fistula is identified by injecting methylene blue (two parts), and hydrogen peroxide (one part); the various ramifications of the tract will be stained, and may be readily identified also. A grooved director is now introduced through the external opening, and insinuated through the tract up to the muscular coat, or as far as it will go with ease. The overlying tissues are incised, and the entire tract is completely dissected out but only as far as the bowel wall. A flexible probe is now passed from within the anus outward into the wound, and bent so as to remain in place. The main portion of the tract is now severed from the muscular coat. A double strand of heavy silk is now threaded through the internal opening by means of the probe which was left in place. The skin and mucosa overlying the muscle beneath this silk ligature are severed, and the ligature drawn down snugly but not tightly on the muscle. The ends of the ligature are left long.

The wound is now packed in the usual manner; the packing is removed in 72 hours, and changed daily or every other day. In the after treatment it is most important to avoid bridging of the sides of the wound and the formation of pockets. Subsequent packings should be inserted to the depth of the wound, but inserted lightly. After two or three weeks all packing is discarded.

The extensive dissection necessary in this operation has deprived the sphincter of much of its support and fixation. To cut the muscle at that time would allow its ends to retract widely, and even dip into the open wound. As the wound has filled in it has given new support and fixation to the sphincter so that it may be severed, and the small tract occupied by the silk thread curetted without the wide separation of the muscle. The sphincter heals promptly with only a narrow partition of fibrous tissue. Function is practically normal. This second stage may be carried out under local anaesthesia.

It may be claimed that this two stage operation may be carried out without the use of the silk thread, the "seton", but that is not true in practice. The mucosa may heal over and obscure the internal orifice making careful dissection necessary for its identification. A closing over of this orifice may be deceptive in that it suggests healing, which is not true.

In 119 patients treated by this operation the author obtained good results, and preserved normal sphincteric action in all cases.

Nelson M. Percy.

CHRISTOPHER, FREDERICK.
Iliac Carcinoid. Case Report with Obstruction, Resection and Recovery. Surgery, Gynecology and Obstetrics. Vol. LVIII, No. 5, May, 1934, pp. 903-905.

The author reviews the literature on iliac carcinoid and reports a case with obstruction, resection and recovery. This tumor occurs most frequently in the obliterated type of appendix vermiformis, next in the ileum, then the colon, rectum and Meckel's diverticulum. They usually do not metastasize. The symptoms are usually produced by the varying degree of intestinal obstruction which they cause.

The author's case, a female, age 55, complained of severe intermittent attacks of epigastric pain. She had had those attacks at irregular intervals during the preceding three years. X-ray examination revealed a gross lesion "somewhere near the ileocecal junction." "The type of obstruction is a matter of conjecture from the X-ray standpoint." At operation "a greatly narrowed portion of bowel" about eight inches from the ileocecal valve was found. The intestine proximal to that point was distended, while distally it was collapsed. About 21 centimeters of the small intestine were excised and a side to side anastomosis performed. Microscopical examination of the excised tissues warranted a diagnosis of annular carcinoid tumor to the small intestine with incomplete obstruction and sub-acute lymphadenitis of the regional mesenteric lymph nodes. The patient recovered uneventfully. Nelson M. Percy.

SECTION VII—*Surgery of the Lower Colon and the Rectum*

HIGH RECTAL PAIN*

AN ANALYSIS OF ONE HUNDRED CASES

By

LOUIS A. BUIE, M.D.

and

JOHN C. M. BRUST, M.D.

ROCHESTER, MINNESOTA

SUCCESS or failure in making a diagnosis often is determined by the ability of the patient to describe his subjective symptoms. We have no way of learning the true nature of the discomfort unless the patient is able to tell us. Often such discomfort, although quite real to the sufferer, definitely cannot be located by him, and he is unable to convey a satisfactory idea concerning it to anyone else. In proctology, usually most symptoms definitely can be described and located. For example, the pain of anal fissure, thrombosed external hemorrhoids, prolapse or of the infected anus with spastic muscles is characteristic; an accurate impression of such can be conveyed to the investigator.

In the course of our routine work often we are called upon to examine patients who complain of distress indefinite in character and in situation. Unfortunately, patients can tell us only that they have "rectal" pain. This pain may be the typical discomfort of an anal fissure, but also it may refer to distress in the lower sacral or coccygeal region which the patient names as "rectal pain", possibly because of his experience at the hands of a physician who has told him of some peculiar rectal disorder. Many physicians, especially those who are unfamiliar with the characteristics of the *normal* anus and rectum, are prone to attribute some such pain to a supposed lesion which they believe exists in the anal canal. A brief study of the neuro-anatomy of the anus and the rectum will refute the belief that hemorrhoids, hypertrophy of anal papillae, fissures, infected crypts, or any other type of anal pathologic change can be responsible for the presenting complaint.

It is necessary, therefore, to go much farther than to accept the simple statement from the patient that he is suffering from "rectal" pain. We have been impressed with that peculiar type of discomfort which is described as being "up inside the rectum". In fact, our inability to determine what is meant by this type of discomfort is responsible for this review.

We have selected records of 100 cases from the files of The Mayo Clinic in which patients complained of distress which was indefinite but finally was stated as being inside of the rectum, usually about a "finger's length from the outside". The entire clinical record of each patient carefully was studied in an attempt to account for the presence of the discomfort. This paper embodies the results of our investigations.

Anatomic Considerations: The anal canal derives its *nerve supply* from the third and fourth sacral nerves and from the hemorrhoidal branch of the pudic nerve. This innervation includes that part of the intestine exit which has, as its inner margin, the pectinate line or *linea dentata,* the perianal margins and the external *sphincter ani* muscle. Such a profuse distribution of sensory nerves readily explains the extreme sensitiveness of the anal canal, and especially of the papillae of Morgagni situated at its upper limit. Above this level, however, the rectal wall is entirely insensitive to pain; it is not possible for any lesion which involves the rectal wall without extension into the adjacent pelvic viscera to produce pain. A rectal polyp may be destroyed by cauterization without the use of anesthesia.

If, therefore, we realize that such nerve distribution is constant, it hardly seems just to urge a patient who complains of discomfort of such indefinite character to submit to the correction of a more or less insignificant and meaningless anal lesion in the hope of relieving pain, assumed to be due to such minor anomoly. Where, then, are we to find the cause of this pain? In Table 1 we have listed, for convenience, the diagnosis on dismissal and the sex, age, and average duration of symptoms in patients complaining of "rectal" pain.

ANALYSIS OF PATIENTS STUDIED

The most interesting, and at the same time the most disappointing, discovery which followed the study of these groups is the fact that the cause of pain was not found in 71 per cent of the cases. It should be repeated that the pain was quite real and often definitely located by the patient as being within a "finger's length" of the anus and up inside the rectum. In spite of this, however, no anal or rectal condition was found which could explain the discomfort. The fact that some type of neurosis, neuralgia or nervous exhaustion was believed to be the underlying basis for most of the complaints is discouraging, not only to the patient, but to anyone who conscientiously endeavors to relieve distress.

A further cross-analysis of that group of cases in which there was a "functional" background only, re-

*Section on Proctology, The Mayo Clinic; by the Head of the Department and the Fellow in Proctology, The Mayo Foundation, respectively.
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TABLE I

Summary of Cases of Rectal Pain

Diagnosis or Disorder	Patients			Average Age, Years	Average Duration of Symptoms, Years
	Total	Male	Female		
Cause of pain not found	19	7	12	43	5
Neurosis	1	1	0	45	5
Rectal neuralgia	1	1	0	31	2
Chronic nervous exhaustion	26	5	21	43	4
Rectal neuralgia	12	6	6	48	4
Psychoneurosis	12	6	6	45	3½
Tabetic rectal crisis	8	8	0	49	2½
Radium (factitial) proctitis	5	0	5	53	6 months
Prostatic disease	6	6	0	43	2
Coccygodynia	1	1	0	45	4
Sacrococcygeal arthritis	2	2	0	52	1
Pelvic tumor	3	0	3	48	2
Adenomyoma of recto-vaginal septum	2	0	2	30	2
Cystocele and rectocele	1	0	1	38	1
Chronic pelvic inflammatory disease	1	0	1	39	4

vealed that twenty-six patients were males and forty-five females. In twenty-six cases the diagnosis of chronic nervous exhaustion was made and, in this subgroup, five patients were males and twenty-one were females. Such a preponderance of females closely parallels the ratio for functional affections in general. In a large series of cases in which the diagnosis was chronic nervous exhaustion, Macy and Allen found that 78 per cent of the patients were women. A careful study of the case records in our series would tend to corroborate the functional aspects of the diagnosis. For example, in the seventy-one cases in which an anatomic diagnosis was not made, eleven patients had migraine, sixteen presented the so-called "irritable bowel" syndrome, four experienced insomnia, twenty-three mentioned an undue tendency to fatigue, thirty-seven recorded constipation as a major disorder and five women had symptoms associated with the menopause.

There was considerable variety in the *type of distress* described by patients with this type of functional distress. There was, however, one attribute which was practically constant and that was *discomfort "up inside" the rectum*. For the most part, the patients spoke of dull, aching, or throbbing pain. It is curious that often they were able accurately to locate the site of the pain, even going so far as to say on which side of the rectal wall the distress was situated. Many stated that the pain began in one small spot and gradually spread until it involved a large part of the rectum. Thirty-eight patients of this so-called "functional" group had undergone various types of anal operation since the onset of their rectal symptoms.

In this group of patients the history should be carefully investigated. We are prone to blame a previous operation for the disturbance; on this account, if for no other, we must endeavor to establish definitely the time of onset of the disorder. In all thirty-eight of these cases symptoms *antedated* the first rectal operation. Only two patients reported relief following operations which included hemorrhoidectomy, surgical treatment of crypts and treatment of hemorrhoids by injection. One may not be critical of those who perform such operations because we have no way of knowing what were the pre-operative findings. However, one can learn from such experiences that he should at least pause before proposing or attempting to offer relief for these indefinite pains by means of operation on the anal canal, though a pathologic lesion may be quite prominent. It is hardly conceivable that even an extensive malignant growth of the anus could produce the indefinite type of discomfort to which we have reference in this paper. It is discouraging for one to be compelled to make such a statement, especially when he himself is unable to offer a solution of the problem. A most painstaking evaluation of symptoms is necessary if the explanation for such distress high in the rectum is to be forthcoming. After such a study, however, physicians either are not able to ascertain the cause in a large proportion of cases, or they find it necessary to attribute the pain to that unknown human quality which is termed an "unstable mechanism".

TABETIC RECTAL CRISIS

Between 1920 and 1933, eight cases of tabetic rectal crisis were observed at this Clinic. In the literature such a subjective manifestation of syphilis has received scant attention. All eight patients in this series were men: their ages varied from thirty-seven to fifty-eight. Rectal symptoms had been present for from two to three years in all cases. These complaints, considered alone, were complex and baffling. The pain usually occurred periodically. Three of the patients stated that the discomfort was excruciating and the pain lancinating; that it began "up inside" the rectum and was projected cephalad into the lower part of the abdomen. In these three cases, special emphasis was placed upon the pains being of sickening severity. Three other patients described sensations of fullness and pressure accompanied by tenseness, and the frequent discharge of small amounts of mucus and liquid feces. For six months, one patient had suffered from a constant, heavy, aching pain which had begun in the rectum and had been projected down both legs. Another patient had had excruciating and stabbing pain before, during and after defecation, which event occurred about three times daily.

Although the patient with tabes usually is constipated, only one of these men was so affected. The Wassermann test was strongly positive in seven of the cases: in the one case in which the reaction was negative, analysis of the spinal fluid returned a positive tabetic gold curve. Abdominal and girdle pains were accompanying complaints in two cases; unmistakable evidence of *tabes dorsalis* was present in all eight patients. The competency of the muscular apparatus at the outlet of the rectum was carefully examined in all instances but that type of insufficiency which might be classed as "patulous" anus was observed only once.

FACTITIAL PROCTITIS

"Factitial" proctitis is a lesion within the rectum which results usually from the application of radium to carcinoma of the uterine cervix. As a result of exposure of the anterior rectal wall to the rays, the tissues immediately adjacent to the uterine cervix undergo inflammatory changes which ultimately may break down and form ulcer. In many cases, healing will occur with only superficial changes in the mucous membrane. Characteristic telangiectases are present in a pale, scarred mucosa. When the exposure has been such as to produce breaking down of the rectal wall, there develops a characteristic ulcer of oval shape, with a tenacious silver-gray or yellowish membrane. The new, small blood vessels in the scarred mucous membrane are usually sensitive; they bleed

following the slightest trauma. Usually, the entire diseased region presents limited mobility due to its adherence to adjacent structures; it is probable that this extrarectal fixation, with through-and-through involvement, causes the discomfort. The rectal lesion, which is confined in almost 94 per cent of instances to its anterior wall adjacent to the second valve of Houston, is easily diagnosed by proctoscopic examination.

This lesion was discovered in eight of 100 cases studied in the present series, in which the complaint was high rectal pain. Although bleeding was constant and is always the most common manifestation of factitial proctitis, pain usually is associated. It is a vague sort of distress; commonly, patients experience difficulty in describing as well as locating it; however, a "dull ache" is mentioned by most patients. This discomfort, as a rule, is independent of defecation and is characteristically located high in the rectum. A history of carcinoma of the uterine cervix followed by treatment with radium usually is obtained.

The *prognosis* is dependent upon the outcome of the initial disorder. However, local treatment is helpful and often materially lessens the duration of the discomfort. Local instillations of witch-hazel and warm olive oil, together with the daily use of small, warm, cleansing rectal irrigations, usually are sufficient to keep the rectum clean and definitely to add to the patient's comfort. Healing is very slow. Such rectal hygienic measures should be exhibited as routine even after the local lesion has disappeared. The scarred tissues continue very sensitive and break down following the slightest trauma.

PROSTATIC DISEASE

In six patients, disease of the prostate gland appeared to be the cause of the rectal pain. In these cases, however, there was considerable indecision concerning the type and situation of the discomfort as it was described by the patient. Usually there was a dull, heavy, aching sensation up in the rectum; perineal discomfort frequently was an accompanying complaint. Thorough proctoscopic examinations were made but in no case was anything discovered which might be held accountable for the symptoms. However, special urologic examination, with massage of the prostate gland, ultimately proved that prostatic disease existed. It is not necessary to go into the various prostatic manifestations in these cases except to mention that there was often significant tenderness and the gland itself was enlarged, soft, and boggy. Treatment by massage was given in four cases and relief from the discomfort followed rather quickly. These results confirmed our impression that a diseased prostate gland may be responsible for high rectal distress.

COCCYGODYNIA AND SACROCOCCYGEAL ARTHRITIS

In three cases in which the ultimate diagnosis fell in this category, the patients made the general complaint of pain up inside the rectum. It bore no relationship to defecation and usually was aggravated by sitting or lying down or by pressure on the lower part of the spine. Movement of the coccyx produced pain which might be considered typical. In one case, roentgenograms revealed evidence of sacrococcygeal arthritic changes.

PELVIC TUMORS

Three cases of pelvic tumor were included in the series, all of which presented perplexing diagnostic problems. Proctoscopic examination failed to reveal anything of significance in any of these three cases. In two cases, dermoid tumors of the ovary ultimately were found and, in these, the rectal pain, which was projected suggestively upward into the left side of the pelvis, was relieved when the tumors were extirpated. The other patient had undergone a great variety of treatments which included hemorrhoidectomy and two operations for "fissure". On pelvic examination in this case, a mass was felt in the *cul de sac*, and a markedly prolapsed left kidney was found at abdominal exploration. Nephropexy was followed by complete relief from the rectal pain.

ADENOMYOMA OF THE RECTOVAGINAL SEPTUM

In two women, in the series, each was found to have a mass in the rectovaginal septum. A preoperative diagnosis of adenomyoma was made in both cases. In each patient, the presenting symptoms of rectal pain had persisted for two years; the distress was more pronounced at the menstrual periods. Both patients gave histories of menorrhagia. Thorough proctoscopic examination failed to reveal anything of significance, but digital examination disclosed a nodular mass high up behind the cervix in the rectovaginal septum. Here, again, is an extra-rectal disorder which is productive of symptoms which curiously relate themselves to the rectum alone.

CYSTOCELE AND RECTOCELE

In only one case was it felt that marked injuries during childbirth, with subsequent relaxation of the pelvic floor, had produced pain referred to the rectum. This woman's discomfort always had begun in the rectum; it seemed to spread to the entire pelvis. She had marked cystocele and rectocele, but the clinicians were skeptical as to the significance of these abnormalities and hesitated to promise relief by the usual reparative operation for the correction of the perineal deformity. The operation was performed, however, and, two years later, the patient reported that her trouble had entirely disappeared and that she had no further rectal discomfort.

CHRONIC INFLAMMATORY DISEASE OF THE PELVIS

One woman, who complained of a sensation of "weight" in the rectum, which was partially relieved by enemas, was found to have left-sided hydrosalpinx, with dense adhesions between the left oviduct and ovary and an adherent inflammatory process involving the sigmoid. Removal of the diseased organs and freeing the sigmoid gave complete relief from the rectal pain.

COMMENT

In studying this problem of high rectal pain purposely we have omitted all cases in which there was some primary rectal disorder capable of accounting for the patient's discomfort. We might properly have omitted the eight cases of factitial proctitis, but we include them because of their rarity and because of the fact that they were due originally to an extrarectal disease.

As in functional disease elsewhere in the body, we should approach the problems of such patients with the utmost caution and consideration. All these patients are sick and have complaints which are quite real to them. When we find that the examination of the rectum is negative, we should pursue our investigation exhaustively in an attempt to discover something which will help us to give relief. Many of these patients have a wholesome and justifiable fear of carcinoma, and even in those instances in which relief was not possible, a thorough explanation concerning the *negative* findings, accompanied by reassurance, materially lessened their worries and, peculiarly enough, their discomfort. The tabetic group is interesting and

worthy of a complete study by itself. The condition is comparable with tabetic crises more commonly seen elsewhere in the body; although anti-syphilitic treatment should be instituted, too much cannot be expected in the relief of the rectal pain.

In cases where a definite extrarectal lesion exists, such as prostatitis, adenomyoma, prolapse, sacrococcygeal disease, or abnormality in the pelvis, surgical intervention may be indicated, but even in these patients we should not be too optimistic in our prognosis.

Although a prolapsed ovary did not figure in this group, it is probable that such a condition sometimes will account for high rectal pain. It is then usually of a rather acute nature and is experienced during a time when the rectum is filled.

It is likely that the rectum and the perirectal tissues are subject to the same nervous reactions as are other parts of the body. There seems to be a significant similarity between attacks of migraine and some of the paroxysms of rectal pain which we have heard described. It is necessary to be constantly on guard in such cases, so that we may avoid treatment by surgical measures directed against incidental and meaningless pathologic disorders of the anus. Such measures practically always are futile: the patient recovers from the operation only to find that he is still suffering with the symptoms for which he originally sought relief. A careful evaluation of the history should be undertaken in such cases in order to distinguish the pain of those pathologic changes which can be relieved by operation or by treatment from the indefinite forms of discomfort which we have tried to enumerate and describe in this paper.

It should be remembered that almost all patients indiscriminately speak of "pain in the rectum" when, in fact, such discomfort may be located in the lower part of the back, to the hips, or to the anus, rectum, perineum, or to the coccyx. Such pain may have no relation whatever to the functions of the lower bowel.

ABSTRACTS

BLOOM, DAVID.

Stricture of the Rectum due to Lymphogranuloma Inguinale. Surgery, Gynecology and Obstetrics. Vol. LVIII, No. 5, May, 1934, pp. 827-840.

The author proposed to prove that a certain group of rectal strictures which have been baffling surgeons for a long time are due to a previous infection with the lymphogranuloma inguinale virus.

The problem of this group of rectal strictures is inseparable from that of "esthiomene" described by Hugier in 1848. In 1875 Fournier described the same syndrome under the name of "syphilome anorectal". It is characterized by chronic ulceration of the vulva associated with elephantiasis and sclerosis of the vulva, the anal region, and the rectal wall, the latter producing anal fistulas and rectal strictures.

Because of the frequent occurrence of this syndrome in prostitutes it was thought that syphilis, gonorrhoea and *ulcus molle* were the causative factors. Tuberculosis, frequent trauma and anal infections were thought to be the etiological factor. Because of the frequent association of this syndrome with elephantiasis and ulceration of the genitals and the anal region the same etiological agent was considered for both. From the maze of opinions an important factor stands out as of first importance in the causation of the affection, namely, the previous total extirpation of the inguinal lymph nodes or their destruction due to inflammation and sclerosis. Jersild denied that syphilis was the cause, pointing out that miscroscopically the tissues did not show syphilitic changes, and that anti-syphilitic treatment was not efficacious. He showed that in 60 per cent to 70 per cent of the cases there was an associated elephantiasis vulvae, and the involved tissues both clinically and pathologically were of the elephantiastic nature. He employed the term "elephantiasis genito-ano-rectale", which is frequently designated in the French literature as the "Jersild syndrome". Jersild called attention to the fixed localization of the pathological process in the rectum, and explained its pathogenesis by utilizing the findings of Gerota who emphasized two important points: (1) the ano-genito-inguinal lymphatic system communicates with that of the rectum by multiple anastomoses, (2) in the lateral wall of the rectum, directly on the tunica muscularis, between the latter and the "fascia recti propria", extending from immediately above the insertion of the levator ani muscle at the rectum up to the level at which the peritoneum reaches the lateral wall, there are situated six to eight lymph glands which receive the lymph from the lower portion of the rectum. These glands are called the "anorectal glands of Gerota". They help one to understand why infectious agents in case of obstruction of the ano-genito inguinal system will invade the wall of the rectum. When both systems are obstructed the tissues between them will suffer from chronic lympho stasis. The lymph vessels which leave the rectal wall above the insertion of the peritoneum empty into the mesorectal glands, and are not affected, and therefore there is no reason for the rectal wall in that location to become infiltrated.

While the majority of investigators have come to agree that the etiological factor in the production of those strictures is to be found in the disturbance of the lymphatic flow, there is confusion and uncertainty about the nature of this infectious agent.

The uncertainty and confusion about the etiology of those conditions described as esthiomene, syphilome anorectal, etc., came to an end when Frei suggested in 1927 the possibility of those conditions being due to the virus of lymphogranuloma inguinale. Frei and Koppel proved that assumption by a positive Frei test in a number of cases of obstinate ulceration of the vulva associated with elephantiastic hypertrophy of the vulva, anus and rectum.

Meyer and Rosenfeld excised a granulomatous growth of the labia minora in a case of esthiomene, inoculated it into a guinea pig, and proved the pathological resemblance of the resulting mass with the lymphogranuloma inguinale tissue. Similar lesions have been produced in the same manner in monkeys.

The greatest majority of the strictures are located within the lowest 10 centimeters above the anus.

Symptoms: The patients usually give a history of anal fistulas, muco-purulent and bloody discharge from the rectum, painful defecation, and finally obstinate constipation. Pain and symptoms of stenosis appear late, and are extremely resistant to treatment. The cases are usually diagnosed as cancer of the rectum, then syphilis, and after some antisyphilitic treatment has been carried out without results operative measures are performed. The affection is often fatal. These strictures strongly resemble the "benign rectal strictures", and one may readily conclude that they are identical. Strauss reported in February, 1933, 72 cases of "venereal strictures" of the rectum in which the Frei test was positive in 69 cases.

The author points out that the abundant anastomoses between the lymphatics of the vulva and the rectum in the female explains the greater frequency of rectal involvement in that sex. In the male the lymphatics draining the external genitalia empty into the inguinal nodes and anastomose very poorly with the perineal and rectal lymphatics.

The author concludes that from a review of the literature of "esthiomene" and "syphilome anorectal" on the one hand, and of the so-called "benign strictures" of the rectum on the other hand, a remarkable resemblance in the confusion regarding their etiology is apparent. He believes that most, if not all, of these conditions are identical, and are due to the virus of lymphogranuloma inguinale. He makes a plea to stimulate the interest of the medical profession, particularly the surgeons, in this disease, and for its early recognition and treatment before fibrosis is advanced. The article has 13 figures.

Nelson M. Percy.

SECTION VIII—*Editorial*

The editorial contributions published in this Journal represent only the opinions of their writers. Such being the case, this Journal or the American Association is in no way responsible for editorial expressions.

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

AMERICAN BOARD OF GASTROENTEROLOGY

In an editorial in the March issue of this Journal the writer described the early steps in the formation of our Board. The plans for the Board and its proposed By-Laws having been approved by the Advisory Board for Medical Specialties at its February, 1934, meeting and by the American Gastroenterological Association at its May, 1934, meeting, that Association appointed four members to comprise a joint Board together with four members from the Section on Gastroenterology and Proctology of the American Medical Association. This necessitated the later appointment of a fourth representative from the Section, there having been only three originally appointed. The whole membership of the new Board then consisted of the following: *From the American Gastroenterological Association:* George B. Eusterman, Ernest H. Gaither (Chairman), Sidney K. Simon and Franklin W. White; *from the Section:* Albert F. R. Andresen (Chairman), Henry L. Bockus, Adolph Sachs and Frank Smithies.

Copies of the proposed By-Laws and Articles of Incorporation were submitted to the Advisory Board for Medical Specialties in May, 1934, and were approved by that Board, the Secretary of which, Doctor Paul Titus, stating as his opinion that our Board would be fully approved by the Advisory Board at its June meeting, to be held on the Sunday prior to the American Medical Association's Sessions. We were invited to send representatives to this meeting. Just preceding the meeting a Committee of the Advisory Board suggested a few minor changes in the By-Laws, to conform with standards which had been adopted at a joint meeting of a Committee of the Advisory Board and the Council on Medical Education and Hospitals of the American Medical Association the previous day. Our By-Laws were then declared entirely acceptable.

The first order of business at the national Advisory Board meeting consisted of the reading of a report of the joint Committee mentioned above. In addition to the recommendations regarding standards, the Committee presented a list of the twelve "branches of medicine recognized as suitable fields for the certification of specialists." On this list gastroenterology, and also proctology, were conspicuous by their *absence*. Representatives of the proposed new Boards of gastroenterology and of proctology were then given an opportunity to present arguments in favor of their specialties being included in the list, and for gastroenterology Doctors Smithies, Gaither and Andresen, and for proctology, Doctors Rosser, Buie and Hirschmann, seemed to impress the Board with the reasonableness of their claims. However, it was announced that, in view of the fact that the Council on Medical Education and Hospitals definitely had decided on the list as presented, the Advisory Board could do nothing but accept the report and adopt its recommendations. However, it was made plain that this stand was not necessarily final, but later could be modified if it was found to be advisable or necessary.

Two days after the above meeting, the delegate of the Section on Gastroenterology and Proctology to the House of Delegates of the American Medical Association, Doctor Descum C. McKenney, presented a resolution calling upon the Council on Medical Education and Hospitals to add gastroenterology and proctology to the "list of specialties in medicine and surgery to be recognized for certification." This resolution was referred by the Speaker of the House of Delegates to the Reference Committee on Medical Education. An open hearing by this body was held the next day, presided over by its Chairman, Doctor Irvin Abell, and attended by members of the Council on Medical Education and Hospitals. At this meeting, arguments again were presented by representatives of organized gastroenterology and proctology. These men also were questioned by members of the Committee and of the Council. So impressed were those present with the need for qualifying boards in these specialties that the Committee approved of the Resolution as presented and recommended that the matter be "referred to the Board of Trustees and Council on Medical Education and Hospitals for determination of the methods of examination and certification in these specialties." *This Resolution was adopted by the House of Delegates on the following day, in open session.*

On June 13, 1934, the representatives appointed by the two national societies met at the Hotel Statler in Cleveland, adopted By-Laws, signed the Articles of Incorporation of the American Board of Gastroenterology and elected the following officers: President, Albert F. R. Andresen, of Brooklyn; Vice-President, Franklin W. White, of Boston; Secretary-General, Ernest H. Gaither, of Baltimore; Treasurer, Frank Smithies, of Chicago, and additional members of Board of Regents, Henry L. Bockus, of Philadelphia; George B. Eusterman, of Rochester, Minnesota; Adolph Sachs, of Omaha, and Sidney K. Simon, of New Orleans.

Owing to the fact that the Advisory Board on Medical Specialties has taken the wholly unwarranted attitude that it was "cheap politics" for our Board to adopt the direct, above-board method of bringing the matter of the recognition of our specialty to the attention of the American Medical Association, our Board thus far has refrained from going through with its incorporation. We are awaiting the action of the Council on Medical Education and Hospitals at its October, 1934, meeting, in order that we may fully cooperate with it in the organization of this very necessary Board.

It would seem, after all, that the American Medical Association is the logical organization for controlling the certification of specialists and that it best can accomplish this by cooperating with such qualifying Boards as have been formed by the recognized national organizations in each specialty.

Albert F. R. Andresen (Brooklyn).

THE NEED FOR PRINTING REFORMS IN MEDICAL JOURNALS

The question of typographical format in medical periodicals never has received sufficient public or professional consideration to sanction a policy of emanci-

pation. Such emancipation from the standardized, hard-and-fast principles obtaining in 99 per cent of reputable medical periodicals, sorely is needed if for nothing more important than a concession to eye comfort and to the esthetic demands of physicians long accustomed to and appreciative of elegant arrangement in all other divisions of modern printing.

At an increased cost to the Journal's Management, but without additional financial burden upon its readers, the American Journal of Digestive Diseases and Nutrition in a short time could adopt a typographical format in harmony with the best of modern printing. Indeed such a policy actually is our desire. However, before committing itself to what to medical men may seem an innovation, it is our wish to have an expression of opinion from our readers. Certainly, at the recent "physicians' hobbies" exhibition held in New York, art, in its broadest sense, found outstanding exponents in our ranks.

The setting of folio lines at the bottom of pages; the use of 3-point rules to give life and solidity; the employment of extra bold, diversified fonts for themes and titles; symmetrical page arrangement of uniform column-width cuts; the omission of initial capitals but the use of attractive designs for focussing attention; reverse-plate headings for section beginnings; artistic, balanced individual page lay-outs; the use of brief summaries (technically styled "blurbs") which convey at a glance the essence of the article following—these and other changes of format strongly are recommended by qualified advisers (printers, psychologists, ophthalmologists) as most desirable departures.

The conservatism of our profession may view such proposals as out of harmony with the character of this or any medical magazine, but it should be borne in mind that a periodical strictly maintained on the highest possible ethical plane, with regard both to editorial matter and advertising policy, also should lead the way in what eventually must happen to all medical journals: typographical emancipation for the purpose not alone of producing more easily read magazines but also of satisfying one's desire for comfort and pleasure and convenience when reading. One need not detail the advantages to contributors when their not infrequently out-of-the-ordinary or strictly attention-demanding, technical essays are arranged and printed in a fashion which, psychologically, is in the advanced tradition and, typographically, is conducive to the minimum of handicap to concentration and understanding.

In its efforts to give its readers the most representative thought in topics concerning digestive ailments and nutrition, the Journal's management hopes to sponsor, in medical periodicals, those modern principles of format which lay publications of the first rank soundly have developed and established for the benefit of their clientele. However, the "timid" or the professionally conservative of our clan need not become alarmed at this suggested departure from standards, traditional if rather hoary and incommoding. Our attempts to advance medical periodical format from that ancientness which is the wonder—even ridicule—of modern stylists (using this word in its best sense) will not be alarming, precipitate or freakish. Assistance, perhaps not even suspected of being rendered by the doctor-reader until he ponders how unattractive and trying are the medical journals which routinely pass over his desk, is sought and awaited.

May we be favored in this effort at "emancipation" from the long and wearily-borne standardized medical journal format, by our readers' opinions and suggestions? Perhaps some of the letters concerning this proposed departure from slavish custom—much of it, merely thoughtlessness or inertia—can be given space in the Journal's columns.

Beaumont S. Cornell.

THE JOURNAL'S NEW DEPARTMENT "THE CLINIC"

At hospitals, frequently one may pass a most profitable hour in "Doctors' Rooms" listening to "shop" talk. There it is that the puzzling "case" (the unusual in symptomatology, the actual therapy, the unexpected recoveries or deaths, the striking pathology) freely is discussed. Such impromptu "clinics" not rarely teach that much knowledge of medicine and its protean problems escape mention in text-books, journals and hospital records. Not rarely, a trained clinician or teacher of medicine can amplify abundantly his mental equipment by judiciously selecting facts as set forth by a practitioner, who by nature is not alone a shrewd observer and physician, but who, as a consequence of many years of experience in all kinds of circumstances, qualifies as a teacher, even though he holds no institutional "chair."

Some months ago, so well-established investigators and astute clinicians as Dr. George B. Eusterman and Dr. Walter Alvarez, Mayo Clinic, wrote in effect: Would there not be a place in a magazine such as the American Journal of Digestive Diseases and Nutrition for publication of a series of interesting and unusual clinical cases as observed in common, everyday practice, wherein are emphasized, briefly, and in a practical way, how and why diagnoses were made, what therapy was exhibited, what was the result or, if the patient died, what autopsies disclosed? Recital of such cases need not lead their reporters into the preparation of extensive or formal papers—indeed, if such were demanded, many men would not respond, they having neither the time nor the desires to go into matters in detailed manner—but, if men simply would jot down, even on their regular office stationery, the essential facts, the intended purposes would be served. Recital of these isolated cases, these strange or curious anomalies or the results of therapy exhibited by trained, observant and sound-thinking practitioners, who, in every sense of the word are *doctors*, might prove of incalculable benefit to practice in general and to the physician in particular.

Thoroughly appreciating the possibilities in the communications above summarized and the wisdom of the suggestions, beginning with this issue, the Journal has set apart space for "The Clinic". This department is open to all readers. They are urged to make it of the value anticipated in the letters of Drs. Eusterman and Alvarez. Contributors may be assured that the Editor will be most liberally inclined towards the prompt publication of reports which tell clinical tales and carry diagnostic, therapeutic or pathologic messages.

It is advised that reports be submitted typewritten and double spaced. Authors' names will or will not be printed, in accordance with their requests. Illustrations (not exceeding three per report) will be inserted when they add something to the presentation or avoid long, detailed descriptions. When possible, the names of the institutions and cities in which the cases occurred should be given.

It is the Journal's hope that, before long, the space allotted to "The Clinic" will justify continuance of this new section. We anticipate not alone hearty co-operation from our readers but look forward, ourselves, to securing a liberal post-graduate education from the material contributed.

F. S.

ANNOUNCEMENT

The Editorial Council of the Journal welcomes to its Roster Dr. Roscoe R. Graham, Toronto, Canada.

Dr. Graham needs no introduction to the medical profession of Canada, the United States or, for that matter, to physicians throughout the world. He is Associate Professor of Surgery on the Faculty of Medicine, University of Toronto; among other positions and honors of which Dr. Graham at present is the incumbent, is the Presidency of The American College of Surgeons.

With keen anticipation, the Journal looks forward to Dr. Graham's active participation in its affairs. The reader may expect from his pen clinical and investigative reports of greater than ordinary caliber and interest.

F. S.

Transactions of the American Gastro-Enterological Association can be had for the years 1908 to 1932, inclusive (with the exception of 1911, 1912, 1919, 1920), for $1.00 per volume, plus postage. Apply to Dr. Sara M. Jordan, Recorder, 605 Commonwealth Ave., Boston, Mass.

SECTION IX—*Book Reviews*

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

This Journal is not responsible for the opinions, decisions or grouping expressed by reviewers of books or pamphlets. For the guidance of readers, an attempt is made to indicate the relative worth of reviewed material by placing "stars"— in connection with the reviews. The greater the number of "stars," the more agreeably and importantly has the book or pamphlet impressed the reviewer.*

* * * * *Physical Diagnosis*, by Richard C. Cabot, M.D., Professor of Clinical Medicine (Emeritus) in Harvard University, formerly Chief of the West Medical Service at the Massachusetts General Hospital, Boston. Eleventh edition: 540 pp., with a Frontispiece and 317 illustrations, charts and diagrams. Published by William Wood and Company, Baltimore, Maryland, September, 1934.

Brookline *(Boston,* practically though recklessly speaking: actually and very significantly to the *haut monde* Bostonian, distinctly Brookline, the most extensive incorporated village known!) lies securely bastioned rurally by the Welds, Brandegees, Lees, Shaws, the Cabots. Relatively—and locally judged—to the North, Brookline's air-conditioning survives, nay even is protected by, the Saltonstalls, the Lowells, the Hollowells, secure in the enjoyment of their lake-bordered domains. A gentleman's ramble brings the Brookliner to *The* Country Club should he be "westing", while, if he should feel especially leggy and fare Eastward, he comes to the shimmering Charles, its bridge giving upon lovely gardens and leading ultimately, through aimlessly wandering streets, to Harvard Yard itself. Roxbury still remains a barrier of sorts which interposes between the speakeasies and the gangsterdom this side of "The Common", helps to preserve intact the ancient integrity of Brookline, and shunts to the north and east the persistent, route-marching, south Boston Irish and the purse-heavy, ubiquitous Hebrews who thirst for university culture—and, incidentally, aspire to dig in permanently (and do) among the rolling hills, the "promised land", which is East Brookline and Brighton.

Just, as years since, emphasis quite properly was placed upon the wisdom of one's choosing the right ancestors, undoubtedly it follows as a corollary to that axiom, that an individual exhibits superwisdom when he launches an enterprise from a beyond-criticism environment—which Brookline, of course, is. For this bit of New England over-shadows Plymouth's celebrated "Rock" by the *nth* degree carried to infinity. (The blood-directs of the Saltonstalls, the Hollowells, the Lowells, may sniff contemptuous, doubting and adenoidic sniffs at this, but the verity and discrimination of our appraisal stoutly will be maintained by the Cabots, the Welds, the Brandegees, the Shaws, the Lees, with sniffs even more potent because reënforced by hayfever and asthma one or more instance of which ailments occur in each generation of these worthies by actual statistical enumeration).

Hence, when nearly thirty years past, Dr. Richard of the Cabots ("Dick" in the "Yard", to those at the Tavern and even at the Somerset Club!) issued his *magnum opus*, he issued it from Brookline. Moreover, this young man, keen, dome-craniumed, ungainly, confident, energy-bristling, pebble-necked ("Pond's Vanishing Cream" was scorned over that ever-tense *ligamentum nuchae*, despite the advertising of its miracle-working powers alleged to have been substantiated by a member of the clan: by marriage, it's true, and also in exile!)—ran true to type as a Bostonian (Bostonly speaking). Brookline permitted and, mayhap, sponsored the *accouchement* of "Physical Diagnosis, Edition One", assured its unimpeachable legitimacy and, quite possibly, found comfort in the thought that now the village was rather more secure against the Salem-like draughts, which came right steadily—and, most annoyingly—from nor'-by-east, as "that Eddy person" most astonishingly intruded when the Lowells or the Cabots passed the time of day with God.

Most certainly in "Edition One"—and in Editions thereafter—this Richard of the Cabots, shrewdly escaped and antonyminized that widely-repeated classification of fools, which sardonic, stubby, Tippoo Tiblike, gates-ajar-collared, chin-on-cravat, humorous Brother Hugh, urologist Cabot, amusedly created and repeated oft: by no means was he innocent of its publicizing advantages to both the Drs. Cabot. Quite likely, too, Brother Hugh chuckled contentedly whenever he noted how vast were the sums extracted by the Satevepost and other magazines from Brothers Godfrey and Samuel in their efforts to induce folks to spend gold for carbon products, patented roofing-compositions, paints and shingle-stains!

Indeed, Dr. Hugh the austere, but who bears a lively twinkle in his eye, knew precisely the value of his famous *bon mot* on fools; how potent it was as an "ice-breaker" whether in the clinic or when barnstorming medically before provincials (i. e., non-Bostonians) and, incidentally, its profitable potentialities when those familiar with his grouping of "plain fools and damn fools" met Brother Richard, *prima donna* clinician at M.G.H. or came across "Physical Diagnosis, Edition One". The Continental European who expected to find a war-whooping, cursing, vulgar, lustful, maudlin, so-called poet but who, instead, found Walt Whitman a kindly, temperate; soft-voiced, gentle genius, could have received no greater surprise, assumed more favorable attitude to, or receptiveness for, than did the "provincial" when Dr. Richard Cabot briskly entered his hospital amphitheatre. For, with a clarity of thought, crispness and simplicity of language, orderliness of presentation and perfection of technical dexterity, he made the difficult easy, the obscure sharp-etched, stimulated enthusiasm, enquiry and constructive cricitism and held young and old spell-bound hour on hour. As Dr. Cabot sent away his ever-lingering audiences, they buzzed with questionings, were stocked with facts, truths and methods and vocally-eager for the next *seance*.

Although the present generation of medical students and the gray-crowned practitioner may not be aware, for full twenty years following Brother Hugh's oft-told, canny *bon mot* classifying fools, Dr. Richard

Cabot earned, and maintained, undisputed leadership as America's most brilliant, interesting, accurate, lucid, technically efficient, enthusiastic—even self-sacrificing—teacher of medical diagnosis. In truth, seriously it may be questioned if this country ever produced a more beloved, revered clinician, a more capable instructor, a more potent leader, a more extensively appreciated, enthusiasm-creating teacher of post-graduate students. While "Physical Diagnosis" (1905—first edition) carried Dr. Cabot's name and methods country-wide (nay, even world-wide) a not to be neglected factor in his outstanding publicity and, incidentally, his *opportunity* to achieve success, was Brother Hugh's famed classification of fools: students who came to laugh with audacious Brother Hugh remained humbly to learn at the feet of Instructor Richard. And they kept coming and brought hundreds of others.

Richard Cabot's summer school courses under Harvard's auspices created so great a furore in American medicine—especially in the hinterlands—that, long before sessions opened, enrollment books were closed, amid wails of the disappointed. Memorable were those days at South Station and to the thrifty Boston cabbies. To the hack-driver, one need but mention Dr. Cabot's name, and with a grin, a snap of the whip, a cluck to the seemingly-knowing nag, the starry-eyed seeker after knowledge rattled M-G-H-ward. Much bustling about was done by Boston's efficient, if painfully plain, landladies, quite eager to turn an honest penny and ever popping with loquacious gossip concerning the glories of "The Hub", not neglecting those of Dr. Richard and his clinics. Almost religious enthusiasm pervaded the halls and the amphitheatre at Massachusetts General: Cabot the Messiah with the now-ancient Riva-Rocci, pleximeter and Bowles' stethoscope; a mob of practitioner-students, happy, eager, "hypped" in the unique, electric atmosphere and readily responsive to him who "taught as with authority". Mesmer at Paris and, locally, the querulous Eddy at her Commonwealth Avenue citadel staged no more impressive show to no more emotionally exalted audiences than did Dr. Cabot in those euphoric days. Patient followed patient, each a "typical", drifting across just at the right time on the right day, as the card index (patiently and intelligently compiled through the years), functioned perfectly. (Wise, too, were those patients: well they knew their value as "cases"; valuable did they prove in giving hints when, later, as "unknowns" they were parcelled out to students for diagnosis!). Meanwhile, the by-no-means skimpy fees clinked comfortingly into the till of Harvard's Summer School's Treasury—fees, oft enough, accumulated, coin by coin, by the ambitious practitioner "out Union Grove way", but parted with gladly, almost entreatingly.

Aside from what Dr. Richard crammed into his cranium, much joy came to each student from the gabfests in and out of clinics, from Boston's summer-time charm and, most of all, from the course-end's "house party" with "The Professor" as host and the obsequious camera-man making group-pictures of the smiling Master with "his boys"—photographs destined long to occupy places of honor in shabby old offices back home, to be exhibited with pride, to enkindle happy memories and radiate needed stimulus during the long, drab days of grubby practice "in the sticks".

Far off, is the time since Boston was thronged with Brother Richard's disciples. Never again has America seen the like. For two decades the pace continued uncurbed; in truth it became accelerated when the famous "guess courses"—clinico-pathological conferences—were instituted. Meanwhile Brother Hugh had rambled reluctantly to the raw West from his ten-bed urologic service at M.G.H.; probably quite heart-content with his classification of fools, proud of Brother Richard but, withal, possibly not a little puzzled by the vagaries of fate and the whims of Lady Luck.

Perhaps, one here might call attention to the excellent "Physical Diagnosis, Edition One" written by Dr. Richard, sent forth from Brookline and publicized—as, well indeed, was its Author—just at the exact, success-possible moment, by Urologist Hugh. The stage shrewdly was set, the play unique and superb, the audience willingly enthusiastic.

Now to us comes "Physical Diagnosis", Edition *Eleven*. Perhaps in sales it will not prove a "best seller"—even tho' in many respects it should. Especially will it be such if one is attuned to a text-book practically written, published under the eye of an "experienced and sagacious Secretary" and packed as full of facts as a daily newspaper's stock list or as well lined with "stuff" as is the portfolio of a well-established, conservative Boston family whose fortune is "in trust": impregnable, profitable, gamble-proof, rich in "ground-floor initial issues" and guarded with Scrooge-like vigilance.

Some fodder acceptable to medical students and physicians must be available when a text-book scores eleven editions in rather less than thirty years: a reprinting at intervals of approximately two and one-half years. Rarely do figure-pinching publishers send forth books for sentimental reasons alone or in editions so small in numbers as to forbid profit unless such comes from author-subsidy. In this respect, immediately, one would rule *that* "out" if he were at all familiar with the attitude toward non-interest-returning dollar spending of the true Bostonian (i. e., the old "Mayflower" semi-hitch-hikers and their descendants). However heart-warming might be the memories of the crowded days when M.G.H. was a shrine and he was the spirit thereof, reckless cerebration only could conjure the picture of the Author of "Physical Diagnosis"—first or eleventh edition—contracting over his signature to make good any publishing deficit. By nature liberal tho' he be, tradition alone would render such idea untenable! For scientists and scholars as they are these Brothers Hugh and Richard, ever dominant in the Cabots has been the merchant strain, since merchant John, their original American progenitor, in 1700, emigrated from the Island of Jersey with Brother George, a carpenter. The explorer-blood of bold John Cabot storm-hurled upon Newfoundland's rocky coast or that of the French Chabots—"bullheads"—runs not through the veins of the American Cabots, tho' such omission by no means wholly has robbed the Yankee clan of that attribute which the French definition of the original name implies. Just as old "J" and "A" during the Revolutionary War with their letters of marque, boldly swooped down and seized the treasures of luckless ships—and kept them, too—the privateer descendants as "lone hands" roved out of Salem with most profitable results, later, another Samuel grew rich from sending forth "ventures" to China and India and a Frederick set up the stacks of mills to smoke-befog the bright, tho' chill New England air, so have the modern Cabots maintained the hereditary quality of being able merchandizers: hard working, observant for the main chance, self-contained and ever capable of knowing just where were their rock-solid assets. Hence, knowing the blood, one can rest content that each of the previous ten editions of Cabot's "Physical Diagnosis" paid its way and he can have confidence that the Eleventh Edition will not mar the record.

A not negligible reason why this "Physical Diagnosis" finds a ready market is because it comes as a familiar and reminiscence-stirring friend. On one's shelves, one has to look closely lest, in taking down Edition Eleven, he get Edition Three—only the first two editions were lean: since then approximately 550 pages have formed the book. Not alone in appearance is this "old friend" little changed. When one thumbs through its pages words, paragraphs, pictures—many actually memorized two and one-half decades ago—flash forth as do the tales and talks of adolescent days. The opening sentence of Edition Eleven is precisely that of Edition Three; the Section, "The Nervous System", begins exactly in both editions, tho', as some concession to progress, in Edition Eleven, one finds this is Section "XXVII", instead of "XXV"; so it goes, through the entire "revised and reset" present edition.

More than sixty per cent of the illustrations brightening up Edition Eleven similarly illuminated Edition Three and the majority of these also held one's attention in Edition One. Today, as in 1905, the shy, startled, poor little hydrocephalic peeks from behind a drape. However, as a modern touch and due, perhaps, to the watchfulness of the "sagacious Secretary" for the final picture of the book, now a Parkinsonian gentleman apparently not yet indexed in 1905, disconsolately shuffles forward. Cuts revealing modification of Riva-Rocci's ancient sphygmomanometer (how many doctors in this era of the "New Deal" ever have seen one or in how many medical colleges do the museums exhibit this pioneer instrument, its narrow cuff, its provoking trick of losing its mercury?); polygraph tracings, graphs whose data cover the period 1870-1905, reproductions of roentgenograms from the age when X-ray studies were *events*, not as now, such everyday procedures as "walking a mile for a Camel", puzzle and surprise one: so on *ad infinitum*. But this very "old-fashioned" stuff, commands a friendly interest, the enthusiasm of those in whose offices long have hung the faded group-photographs of the cherished Cabot "house-party", admits easy reading of familiar sentences, revives partly forgotten classifications, diagnostic signs, symptoms and allows one, leniently, to pass by the very obvious omissions of newer methods of diagnostic procedure, more exact technique, logical groupings and arrangements.

Not that one may scoff at or belittle Cabot's "Physical Diagnosis", whether it be Edition One or Edition Eleven. Far from it! In the days of his first ambition, his primitive energy, his initial clinical keenness, "der Tag" when all roads led to the Massachusetts General. Dr. Cabot chose what material comprised his book with a carefulness altogether admirable, with a selectiveness—looking back from now—almost uncanny and presented it with an orderliness, consecutiveness and a clarity which appealed mightily to the American student (long befuddled by the obscurities of Vienna's clinics and the wordiness of Sahli, *et al*) wanting "the dope", accurate and without oratory. Scientist-clinician-merchant-Cabot created a textbook after the manner in which the Bostonian establishes a family "trust" portfolio: everything might not be included but what was accumulated was as sound and foolproof as human intelligence, canniness and persistence could make it. No merchant, accountant, broker, banker of old Milk Street ever scrutinized more carefully worthwhile values for his "trust" than did young Dr. Richard search the records of the Massachusetts General Hospital prior to writing "Physical Diagnosis". And, like those shrewd, knowing, Boston men of business, once their portfolios had been established, the family fortune was "set", so Dr. Cabot's original selection of data has proved so thoroughly dependable that, seemingly, as another noted, late, eminent, New Englander, he "chooses" not basically to alter or discard it, even tho', from the viewpoint of a salesman, novelty and more attractive format might prove advantageous. In this regard, he commands both admiration and respect, although assuredly the "modern" Eleventh Edition, typographically considered, is far from being a "Mrs. Jack Gardner's Palace" among present-day text-books.

Not altogether, however, has Dr. Cabot adhered to his 1905 material and groupings. Laboratory technique and the data derived therefrom, quite properly, wholly have been discarded or but casually are mentioned. That, as he approaches the ranks of the Venerable Olympians of Boston or in American medicine, Dr. Cabot has lost interest in what aids the laboratory may furnish, is belied by a recent photograph (Fortune, Feb. 1933, pg. 30) in which he poses appearing astonishingly youthful, with microscope (ancient model), stain bottle (corked and apparently empty) and note-jotting fountain pen (modern). To compensate for omitting the laboratory chapters—they were valuable, too, because they detailed Dr. Cabot's first love: his blood studies, work which he pioneered and through which he became an authority long before he discovered his ability as a throng-magnetizing clinical teacher—he has given us one of the clearest, most concise discussions of practical electro-cardiography yet printed in any language. Here again, what Cabot knows and depends upon he sets forth; what is in the "twilight zone", debatable, misleading, artefactious, he omits.

Before leaving the consideration of this book, a treatise which we have watched with interest—and profit—from its birth to what, among books, is hoary old age, one should not fail to note the extraordinary skill exhibited by the publishers. One marvels at the technique which has brought forth with a clarity even greater than that in 1905, photographs, roentgen reproductions, graphs. So ancient were the garments in which some of the 1905-ers were clad, that it was evident that even at that early date, many photographs were as *passe'* as those of "Uncle Dudley and Aunt Emma" in the old, plush-bound family album. William Wood and Company did a commendable job in 1905 with such photographs and, especially, with X-ray prints from plates; one can bestow no greater praise than to state that, in 1934, down in Baltimore, the Waverly Press actually has improved upon the 1905 originals! It's a remarkable achievement.

To the subject matter, there is a comprehensive index and a complete list which pages each illustration. The type easily is read: the book fits the reader's hand comfortably; it is substantially bound.

This old friend of bookdom, nearly as mature in years as "Osler", quite as epoch-making in its field and equally useful and beloved, goes forth with our cordial good wishes: a good friend, well on in life, faring on new adventures. Firm we are in our faith of its clinical value, its sincerity, its dependability. From thousands of doctors who, for two and one-half decades, trekked to Boston from the very limits of our land for the privilege of "sitting under" Dr. Cabot and who came away enlightened, with sounder ideas, with broader vision and far and away as more competent diagnosticias, Edition Eleven will find the mental latch-string out and the table set for the feast: for together "have we not eaten his salt and broken bread?"

Frank Smithies.

SECTION X—*After "Hours"*

WILLIAM BODENHAMER—EARLY AMERICAN PROCTOLOGIST

By

SIMON B. KLEINER, M.D.*
NEW HAVEN, CONNECTICUT

ONE of the peculiarly fascinating names encountered in reading the literature of proctology is that of William Bodenhamer. In a large number of the publications on rectal surgery, references to this author are constantly encountered. Their constant recurrence arouses a curiosity regarding Bodenhamer, which is well rewarded for the time spent in reviewing his works.

Born in East Berlin, Pennsylvania, in 1808, William Bodenhamer's lifetime carries us from the period of medical darkness preceding Lister, Pasteur and Koch down to the beginning of modern surgery at the time of his death in 1905. His medical education was obtained at the Worthington Medical College of Ohio University, where he received his degree in 1839 (1). However, even before he graduated, Bodenhamer was practicing proctology, for in his first book (2), a letter is published from a patient, Noah Spears of Paris, Kentucky, testifying to the cure of a fistula by Dr. Bodenhamer in the spring of 1837; while a communication from Lewis T. Payne of Woodford County, Kentucky, describes a similar cure in January, 1839.

It is from these published testimonial letters that it is possible to trace the early migrations of Bodenhamer, for references to them show that as late as January, 1842, he was located in Paris, Kentucky, while from 1843 to the fall of 1847 he was active in Louisville. Further statements refer to treatments given in New Orleans beginning in 1847. References to his New Orleans work continue through the winter of 1854, at which time an announcement is made in the Louisville "Democrat" that he has adopted New York as his summer quarters, instead of Louisville as heretofore".

Bodenhamer's first work, "Practical Observation on Some of the Diseases of the Rectum, Anus and Contiguous Textures" (2), published in 1847 at Louisville, was "especially addressed to the non-medical reader". The author states in its preface that he is "disposed to make an apology for the many imperfections of this little work" as it was "written at intervals, *'snatched'* from professional engagements".

At that time Bodenhamer also announced his intention, "at no distant day, to present also to the profession a complete practical work on 'Diseases of the Anus and Rectum', which will contain all that relates to the subject, from the earliest ages, down to the present period, together with the results of his own experience. The work to be illustrated by numerous colored plates, and exemplified by a very large number of cases".

In spite of this promise of a work for the profession, Bodenhamer must have been subjected to severe criticism, for in the introduction to the second edition (3), he writes: "Although the author does not in the present work give his peculiar method of treating those diseases, for reasons already stated, he nevertheless refers with pleasure to his triumphant success in their treatment, as furnishing the most satisfactory and incontestable evidence of its superior excellence. He, however, has no *secrets* on this subject; but will most cheerfully at any time, until his large work appears, communicate his method most freely to any regular physician or surgeon who should feel so much interest in it, as to be induced to call on him."

Well may he apologize, for while his book is intended for the layman, it is far too technical for such readers, including as it does the anatomy and physiology of the rectum and anus, the etiology of various rectal lesions, their symptoms and complications. Historical data also are included—in fact every angle of the important ano-rectal diseases is considered. But when treatment of these conditions is discussed, all methods are frowned upon with the exception of the author's, and description of the latter is omitted entirely in both editions of this, his first book.

In addition to the omission of his system of treatment, the element of fear is introduced in his description to the laity of many proctological procedures (not his own) which were, and still are considered the proper methods of therapy. For example, in describing operative methods of treating fistula, he quotes Colles' lecture in which this surgeon relates that in operating on fistulae, he has more than once seen the knife break, and half the blade left in the wound! And Bodenhamer states that in the treatment of hemorrhoids, excision and cauterization the "cruel, extremely dangerous, and therefore, unscientific measures, * * * and had I more time and space I could here introduce numerous instances, even in our own country, and in our very midst, of the dangerous, as well as fatal effects of these measures".

There are, however, many interesting and instructive chapters in this book. The section devoted to constipation emphasizes the fact that we have not progressed materially in its treatment in the last eighty-five years. He advocates regularity of habits; and exercise; and in referring to proper diet, advises the use of brown bread, bran, ripe fruits such as oranges, figs, prunes, etc., and the drinking of two glasses of water on arising. The use of whole mustard seed is suggested; while the use and abuse of enemata (evidently an innovation in this country at that time) are discussed at length.

*Assistant Clinical Professor of Surgery (Proctology), Yale University School of Medicine.
Submitted August 14, 1934.

In addition to the interest in this work from a medical angle, many of Dr. Bodenhamer's remarks about patients are amusing and interesting from an historical standpoint. For example:

"Case 28. William P. Gray, aged 38, blacksmith, Bardstown, Ky.; cured in the fall of 1843. Mr. Gray was shot dead by R. L. Wickliffe, Esq., on the 9th of August, 1849."

"Case 33. William Montmullen, aged 4, son of John Montmullen, Esq., of Lexington, Ky. This noble little boy was cured in the spring of 1844."

"Colored Persons Cured of Fistula in Ano."

"Case 1. George, aged 45, farmer; cured in the summer of 1842. George was owned by Samuel Wallace, Esq., near Midway, Ky."

"Case 2. Sam, aged 21, spinner; cured in the summer of 1842. Belonged to Horace Coleman of Fayette Cy., Ky., and worked in the hemp factory of Henry Clay, Jr., of Lexington, Ky."

"Case 8. Sol. Patterson (free), aged 44, shoemaker; Louisville, Ky., cured in the summer of 1850", etc.

In spite of his promise to publish a complete practical work for his colleagues, there seems to be no evidence that Bodenhamer ever issued such a work, although quite a few books appeared subsequently. Among them were two monographs, one published in 1850 and quaintly called "A few brief and desultory remarks on anal fistula; being a defence of the author aginst the slanders and misrepresentations of Drs. B. I. Hill, Wooster Beach, and others relative to the treatment of this disease". (4) Another pamphlet was published in 1878 on rectal medication (5), while in 1884 a larger book, "A Theoretical and Practical Treatise on the Hemorrhoidal Disease, Giving Its History, Nature, Causes, Pathology, Diagnosis and Treatment" (6) was issued.

At the time when Bodenhamer began to make his summer headquarters in New York (1854), a second edition of his "Practical Observations" (3) was published, and soon after, in 1859, he located permanently in the metropolis. In the following year, his most important book (7) was published. This work, "Malformations of the Rectum and Anus", was a classic, "gathering for the first time all scattered memoranda of every nation with especial reference to efforts to give relief by operation" (1). In many of the best works on proctology, Bodenhamer's book (7) is cited as authority for certain ano-rectal malformations, and his classification, a modification of Papendorf's, has been used by many rectal surgeons. This book was a true stimulus to the study of rectal diseases from a scientific standpoint.

The classification mentioned above is most interesting in that while it divides malformations of the region into nine different groups, all the malformations classified are those either of absence, narrowing or abnormalities of position of the anal orifice; or of abnormality of the vagina or urethra, because of their opening into the rectum, etc. The peculiarly significant fact to the physician of today is that no mention at all is made of megacolon. It was not until 1888 that Hirschsprung described this condition.

In this book Bodenhamer gives the histories of 287 different cases. In many instances the operative methods are described, and there are 26 excellent lithographed plates descriptive of the malformations, operations and dissections, as well as of the instruments used at the time. The bibliography of this work is most comprehensive and lists several hundred references to malformations of the types classified. It is indeed a book which can still be useful as a reference.

Bodenhamer's monograph "On Anal Fissure" (8) published in 1868, describes, in addition to the etiology, pathology and diagnosis of this condition, the different kinds of treatment then in use, including his own method. Some of his observations are most interesting and instructive, and this work too is still of great value. Certainly some of his advice is acceptable today. For example, he deprecates forcible stretching of the external sphincter as a method of therapy in fissures; and, while he himself favors most conservative treatment, such as the use of cleansing, caustics, slight dilatation, or even incision *to* the muscle fibers, nevertheless, he does not look with absolute disfavor upon our present approved method of treating chronic fissures, namely excision of the ulcer and incision of a few fibers of the sphincter. Still being of the opinion that fissure or ulcer of the anal margin is a lesion of the mucous membrane, Bodenhamer feels that if surgery is used, simple excision of the lesion down to the muscle fibers should be sufficient.

This type of operation the author attributes to Velpeau. The name of this surgeon, better known to us through his method of immobilizing the clavicle, is encountered several times in Bodenhamer's writings, as are the names of Brodie, Morgagni, Basedow, Dupuytren, Nelaton, Colles, and other clinicians who are usually associated with entirely different fields of surgery than the anus and rectum. The numbers of such names as are met in reading Bodenhamer's writings are tacit evidence of the huge amount of literature with which he must have been familiar. It would indeed be most fascinating to delve into their works and find their ideas on rectal surgery.

The section devoted to "physical exploration, diagnosis, and prognosis" in anal fissures is most interesting. The first paragraphs, dealing with ocular and digital exploration, might well be given to every hospital interne as advice on preparation of patients for all rectal examinations. His instructions upon position, method of procedure, etc., are most precise, and in many respects up to date even today. With our modern examining tables in office and clinic, the medical student of today is often at a loss when left to his own resources in making a rectal examination in the sick room.

After calling attention to the frequent presence of a "polypiform body, varying in length from two to eight lines, and of different forms" in cases of chronic fissure, Bodenhamer continues with a description of the methods of digital and instrumental examination. This is quite similar to his description of examination described in his later work on "The Physical Examination of the Rectum; with an Appendix on the Ligation of Haemorrhoidal Tumors" (9). Both books describe the use of the bivalve speculum, and the trivalve trellis speculum, the latter being an invention of Bodenhamer. This instrument is rather ingenious, being small when introduced, while expansion of the blades is controlled by rotating the handle.

He also describes the blunt gorget, a single-bladed speculum, inserted with the finger in its concavity as an obturator. Interest in this instrument is also stimulated by his description of Colles' introduction of a conical piece of polished boxwood as an obturator which is used with the gorget.

The later book (9) describes "recto-colonic" examination, illustrating an early sigmoidoscope, or as he calls it, a "recto-colonic endoscope", fourteen inches long, with a flexible end. This instrument is similar to

the sigmoidoscope of Rehn (10), but it was introduced into the rectum over a flexible whalebone conductor. A reflecting mirror, similar to a laryngoscope was used to see beyond the curves, and illumination was obtained by means of a lamp with a reflector and lens, "used for gas, oil, or any other illuminating material".

A most interesting part of this book is the statement made in connection with his description of examination by the use of trans-illumination—"Splanchnoscopy or Translucency". In describing this method, Bodenhamer tells of Millot's introduction into the stomach or rectum of "glass tubes, of small caliber, containing two platinum wires connected with electrodes of the galvanic apparatus of Middeldorpff". He says further, "in this manner an intense illumination may be transmitted into the visceral cavities, rendering them translucent. At any rate, this artificial illumination, even if it does not result in rendering the walls transparent or rather translucent, might be available in exploring or in operating upon the rectal, vaginal, buccal or nasal passages". This truly was a thought fifty years ahead of his time!

There is also an account in this book about Richardson's experiments describing observation of the bones of a child's wrist and movements and outlines of the heart by means of a specially constructed lamp. When it is remembered that these works were described in 1870, the foresight and vision of Bodenhamer seem all the more remarkable.

His many papers published in the journals from 1879 to 1905 range from the discussion of hemorrhoids in animals (11) to "Some interesting and curious incidents in the history of anal fistula; including celebrated persons who were subject to it" (12). In this paper there is related for a second time the history of the case of Louis XIV; of the attempted cures of fistulae at various spas; and of other experiments over a period of a year by persons with this lesion who were dispatched by the monarch to different places to see if they could obtain a cure without surgery. After all of these experiments had failed, the king finally consented to the operation, which resulted in a cure. The total of the fees paid to the surgeon and his assistants was carefully added up by Dr. Bodenhamer and compared with the fees paid to surgeons in the nineteenth century. As a matter of current interest they are again repeated:

Monsieur Felix (the surgeon) 50,000 crowns	$30,000
Dr. Daquin, 100,000 livres	20,000
Dr. Fagon, 24,000 livres	5,000
Monsieur Bessiere, 40,000 livres	7,500
Four apothecaries, each 12,000 livres ($2,500) total	10.000
Mons. Raye (apprentice to M. Felix) 400 pistoles	1,000

There is no doubt that this was indeed a royal fee, being a total of $73,500!

Dr. Bodenhamer's last paper, "Atony of the Rectum and Sphincters: Its Aetiology, Pathology, Diagnosis, and Treatment" (13), appeared in 1905, shortly after his death. From his writings, Bodenhamer appears to have had an enormous fund of knowledge of proctological literature, and his practical experience must have been equally as large. And while all may not agree with him, especially in his leanings toward too conservative methods in rectal surgery, there is no doubt that his work was a valuable stimulus to our early proctologists.

In the introduction to the very books (2, 3) in which he has been accused of deviating from the ethical path, he gives an excellent recipe for the cure of this evil in proctology—"Did surgeons devote half the time and attention to this class of diseases, which they bestow upon some others of less importance, and did patients consult none but those whom they know to be qualified, *quackery*, in these instances, would at once cease, and *Messrs. Humbug*, that large and flourishing *Firm*, would soon be compelled to close doors."

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SECTION XII—"*The Clinic*"

Brief, practical contributions to this Section are requested from practitioners and investigators, generally. Submitted data will be printed when they "tell a story", emphasize points in diagnosis, therapy or pathology, suggest new instruments or methods of procedure or record the unusual. When possible, contributions should not exceed twelve hundred words each.

IMPALEMENT OF RECTUM; OPERATION AND RECOVERY*

By

MARTIN S. KLECKNER, M.D.†
ALLENTOWN, PENNSYLVANIA

THE ano-rectal region frequently is subjected to various injuries but, numerically, relatively they are infrequent when compared with the other affections of the anus and rectum for which relief is sought. Usually, these injuries result from direct traumatism, foreign bodies (swallowed or introduced), "overenthusiastic" operators, gunshot wounds, impalement, overdistension of the bowel by compressed air, etc.

"Impalement" was a form of punishment practiced by the Orientals and the Romans, but today we see it as probably the most common etiologic factor in injuries of anal zone. The impaling object usually is the sharp, smooth, or protruding part of a fence paling, a pitchfork or an iron standard, which has been forced into the anus, rectum, or near-parts when the patient has slipped or fallen. The course of the impaling agent is influenced in direction and extent by the bony pelvic girdle. The height of a fall and the weight of the individual have an important bearing on the severity of injury inflicted. Commonly there is produced only an extraperitoneal, rectal wound but when intraperitoneal injury complicates the trauma the prognosis becomes serious because infection (particularly the colon bacillus and occasionally the tetanus bacillus) in addition to foreign bodies are introduced into the peritoneal cavity. The adjacent viscera, particularly the bladder, may suffer destructive lesions as the impaling instrument advances.

Should the rectal wall be intact and the injury is below the level of peritoneal reflection, adequate drainage and the usual surgical, nursing and dietetic care promise recovery. Prompt and careful proctologic examination must be made to rule out a perforated viscus. If such has occurred, immediate laparotomy with suture of the tear in the rectal wall, when possible, and adequate pelvic and rectal drainage, give the most favorable prognosis. Shock may be severe and require treatment initial to operation. Hemorrhage is generally internal when visceral perforation occurs; very little evidence to account for such may be seen on proctoscopic examination. With delayed diagnosis and operation, peritoneal sepsis with resulting high mortality are bound to supervene. It is interesting to note that many of these patients, after sustaining severe injury, experience relatively little pain and even may walk considerable distances. These factors may mislead many as to the existence of a serious lesion. The following case is an interesting example of intraperitoneal rectal injury ("impalement").

Case Report: D. J. (No. 72498), age 20, single, lineman for a telephone company, while descending a pole made a misstep when about six feet from the ground and fell upon a "tripod flag standard" which had been carelessly left too close to the pole. (The standard was a tripod with an extension rod having an eye at the tip to which was hooked a chain bearing a warning flag). The rod was thrust up into the patient's rectum but was pulled out by the patient himself; he said it penetrated fully six inches. He was taken to the Allentown General Hospital (Pa.) *via* automobile, a distance of a mile, but he walked into the dispensary.

The patient complained of "low abdominal pains, pain in the rectum, weakness and a desire, but inability to void". He was admitted to the hospital where I saw him one hour after the accident. He was moderately shocked; temperature 97.2 degrees F.; pulse 80 and respiration 20.

Abdominal examination revealed some (moderate) muscular rigidity with average tenderness in the suprapubic region. *Proctologic examination* disclosed no external evidences of injury but internally and on the anterior wall of the rectum, about four inches from the anal orifice, was a small area about one-third inch in diameter which bled slightly. Above this point, for a distance of two inches, were several areas of abraded mucosa, but probing in all places did not reveal a passageway through the rectal wall. As immediate treatment, these areas were touched with 10 per cent silver nitrate solution and then one ounce of 10 per cent neo-silvol solution was gently injected into the rectum. Within a few minutes the patient complained of severe cramp-like pains in the suprapubic region and the left iliac fossa. These symptoms appeared to warrant a diagnosis of a perforated viscus. *Catheterization of the bladder* returned 12 ounces of clear urine—(the specimen was examined at once and found normal).

While the patient was being treated for shock (which included hypodermoclysis of physiological saline solution and caffein sodium benzoate intramuscularly) blood counts were made. The first of two blood counts showed hbg., 95 per cent; r.b.c., 5,200,000, and coagulation time 3 minutes, with w.b.c., 19,900; Polys.-84; Lymph.-11, and Mono.-5. One hour later the second count was w.b.c., 23,600; Polys.-89; Lymph.-8; Mono.-3.

Operation: The patient responded well to treatment for shock and within three hours after admission to the hospital, laparotomy was done under Nitrous-Oxide-Oxygen anaesthesia. Upon entering the peritoneal cavity, some free milky fluid exuded (cultures taken and later reported positive for *B. Coli*). This fluid may have been leakage from the rectum because examination disclosed an irregular tear in

*Read before the Annual Session of the American Proctologic Society, Cleveland, Ohio, June 11-13, 1934.

†From the Surgical Clinic of the Allentown General Hospital.

Submitted August 4, 1934.

the upper rectum; this tear was about one inch in length, running across the right antero-lateral portion; it bled freely. Inasmuch as the injury was located where the peritoneum is reflected from the rectum onto the bladder, hemostasis and attempt at closure of the ruptured gut (catgut and linen) were done under considerable difficulty and after observing the usual surgical technique and walling off the surrounding tissues. No visible evidence of traumatism to any other viscus was found, nor were any foreign bodies present in the abdominal cavity. After placing one rubber tube (¼") in the *cul-de-sac* and one cigarette (Penrose) drain over the region of the tear, the wound was closed in routine manner. One stiff rubber catheter had been inserted into the rectum for a distance of four to five inches above the operative site prior to the closure of the abdominal wound. Unfortunately the interne on duty removed this catheter the next day because "it was annoying to the patient"; such carelessness greatly complicated our treatment.

For four days hypodermoclysis and morphine (in sufficient amount) were continued. The incision broke down nine days after operation and a fecal fistula formed but adhesive strapping helped remedy this condition. Five weeks after the accident, the fistulous tract had healed, the patient was having normal bowel movements and was out of bed. He was discharged from the hospital seven and one-half weeks following operation.

A year later, a small incisional hernia was repaired with good result. One and one-half years after the patient's accident, a pilonidal sinus of average degree was first noted. This I excised and packed lightly. Healing was complete in two months. The latter condition while never complained of, prior to the patient's accident, had no connection with the impalement. We mention it because it might provide an interesting medico-legal point to the average jury should this patient appear in a court for the purpose of securing "damages".

TOXIC CIRRHOSIS DUE TO CINCOPHEN; RECOVERY*

By

HENRY F. KRAMER, M.D.
BROOKLYN, NEW YORK

CASES of liver necrosis following the use of cincophen and allied chemicals have been reported. In a recent paper *(Archives of Internal Medicine)*, Weir & Comfort gathered 98 cases of this complication from the literature up to November, 1933, and added 19 cases of their own, a total of 117.

The following case is reported because a complete work-up was possible, including histological examination and because of the rapid improvement following omentopexy.

Case Report—Mr. J. A. C., age 63, entered the Brooklyn Hospital, August 23, 1933, complaining of: Fatigability (4½ weeks), yellow tinge to skin and eyes (3 weeks), increasing abdominal girth (2 weeks).

Present Illness: Began on July 13, at which time he noticed for the first time that he was exhausted after a day's work. This circumstance continued for one week and then patient sought medical aid. A negative report was given. Four days later the skin became tinged yellow, there was a diminished zest for food and greasy foods disagreed. Other symptoms were belching, constipation and heartburn. He lost 10 pounds in one week beginning July 22 to 29, noting that arms seemed thin while his girth increased. Never were there pain, headache, tinnitis, dizziness, trembling, pyrosis, nausea, chills, fever, vomiting, hematemesis, bad taste in mouth, sweating, tenesmus, diarrhoea, dyschenzia, excess flatus, tarry or bloody stools.

In this patient's experience the ailment was the first attack of this character. For 25 years patient has had four bowel movements daily, semi-formed, brown. For a period of a few weeks before this present illness patient was taking cincophen tablets for pains in his legs; in all about 20 to 30 tablets were taken. This medication was forgotten when

*Submitted September 18, 1934.

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the patient was first questioned and the fact was not brought out until after operation.

Past History: Patient states that he has had an exceptionally fine constitution, a vigorous athletic life and has been active in work.

Medical: Influenza followed by pneumonia in 1918. No pleurisy. Pneumonia in 1915. No typhoid fever or rheumatism. Malaria for five years between six and ten. Tapeworm at 20 cured by malefern.

Surgical: Incision and drainage of knee and thigh for "blood poisoning" at Brooklyn Hospital 15 years ago. Five years ago had a perineal operation on prostate following trauma which resulted in retention of urine. Frequent dislocations of shoulder, elbow and left knee. Fracture of skull 22 years ago.

Childhood: Measles, mumps, chickenpox, diphtheria, no scarlet fever. Abscess of ears in childhood. Said to have had tuberculosis at 16 years of age, cured by living in the country. No cough, hemoptyses, sweats or sputum for 20 years except when he had upper respiratory infections.

Gastro-Intestinal: No symptoms except for present illness. He admits chronic overfeeding.

Genito-Urinary: At 22 pyelitis for five months, experienced pain in both kidney regions. No children. Denies lues and gonorrhoea.

Neurological: No syncope vertigo, unconscious, convulsions, paralysis. Not nervous. Wife living and well.

Family History: Mother died of pernicious anaemia, tuberculosis, and cancer. One brother died of tuberculosis, another of croup. Father of quinsy.

The patient was born in Staten Island but lived on the Atlantic seaboard all his life. Trips to Europe twice a year. Visited the tropics only once (Africa; Algiers in 1919 for one week). Silk importer, married 15 years. Tobacco, 12 cigarettes daily. Alcohol, up to three years, drank anything and everything.

Physical Examination: Large, well-developed and nourished portly white male. Deep jaundice of skin and sclerae. Hypopituitary type. Except for *jaundice* the skin generally is clear and is somewhat loose on arms, neck and thighs. *Head:* moderate alopecia; *sinuses* not tender.

Eyes: sclerae, deep yellow; pupils react to L and A; no nystagmus; corneal reflex present. *Nose:* left spt. deviation with hypertrophied turbinate. *Ears:* negative-pinnae and mastoid zones. *Mouth:* one upper canine present; retracted, unhealthy gums; pus at gum margin; two lower left canine and first premolar; these teeth too are exposed due to retraction of unhealthy gums.

Tongue: moderate grayish coat; *pharynx* and tonsils clear; palatal reflex present bilateral. *Neck:* negative for nodes; thyroid, negative. *Chest:* deep, no deformities; good lung resonance throughout; a rather persistent shower of medium moist and musical rales heard over both bases in posterior axillary lines; probably adventitious; voice and breath sounds and tactile fremitus normal; the diaphragmatic dome on the right anterior comes to fourth rib, therefore, a little high; diaphragm excursions are normal by percussion. *Heart:* rate slow rhythm, regular, quality good, no thrills, shocks, or murmurs; apex in fourth space, well within the line. *Blood Vessels:* moderate sclerosis and increased tension as radials. *Lymphatic* system - cervical supraclavicular, axillary popliteal or epitrochlear glands palpated.

Abdomen: No spasm; a bulge appears in midline from xiphoid to umbilicus on straining; the recti muscles are spread widely here but no frank hernia present; no hyperaesthesia; moderate tenderness to deep palpation in both upper quadrants. Abdomen is obese and presents a bulge corresponding to epigastrium and medium portions of both upper quadrants. This gives flat note on percussion and is but vaguely outlined by palpation. Firm, rather smooth, to right of the epigastrium there is a mass the size of a small grapefruit, deep and quite unmovable; hard, tender, not nodular, its borders are difficult to define. Liver descends two fingers below the costal margin. Fluid wave is present.

Laboratory Reports: Rehfuss test of gastric contents:

T.	10	35	60	52	43	40	38	32	18
F.	4	30	55	50	40	32	35	28	10

Negative for blood; lactic acid, and Boas Oppler bacilli.

Urine: Bile positive; trace of albumen.

Stool: Positive bile and occult blood.

Blood: Icterus index—100-42; Vandenberg—biphasic; Wassermann—negative.

Blood Sugar: 240.8 mg. per 100 c.m.; R. B. C., 4,680,000; diastase activity of blood, 29; W. B. C., 7,500; bleeding time, one minute; coagulation time, five minutes; Hgb., 92-88 per cent.

Blood Pressure, 110/50.

Summary of X-ray Gastro-Intestinal Series: Broad looping of the duodenum, also an enlargement and looping of the upper jejunum as from peri-duodenal and peri-jejunal adhesions, plus the presence of pancreatic enlargement. The loops of the ileum are lifted out of the lower pelvis (ascites). Twenty-four-hour intestinal hypermotility, evidently of reflex origin.

DIAGNOSIS: Peri-duodenal and peri-jejunal adhesion, suggestion of pancreatic enlargement; ascites; spasm of descending colon and sigmoid angle.

Laboratory examination of ascitic fluid shows no evidences suggestive of tumor process.

Operation: Exploratory laparotomy; biopsy omentopexy. Three-inch right rectus incision. Two gallons cloudy, yellow fluid aspirated. The round ligament contained many large vessels. The *liver* was found to be about normal in size but its surface was rough and finely nodular, a reddish slatey gray in color, and hard to palpatate, but tender and friable when biopsy was done. The *gall bladder* felt normal, without stones. The *pancreas* and *pylorus* felt normal. The *spleen* could not be reached. The *omentum* was drawn out until when spread it covered a circle about four inches in diameter, and was tacked in the spaces between rectus-posterior sheath, rectus-anterior sheath and a little in the subcutaneous fat. Skin closed with interrupted black silk. (Operation by Dr. W. H. Field.)

Section of liver (October 5, 1933). Gross—a cuboidal fragment of liver 1.5 cm. in diameter. On section the cut surface is coarsely mottled in yellow and gray.

Histological: There is complete necrosis of all liver cells throughout the material removed. The liver cell-bodies are transparent, except for granules of bile pigment. The connective tissue about the portal canals is moderately increased in amount. There are scattered areas of bile-duct proliferation. No evidences of inflammatory process are apparent.

COMMENT

Since leaving the hospital this patient's symptoms have gradually improved. The hemoglobin and weight have returned to normal. The ascites has entirely disappeared. Clinically this case represents the severer form of toxic cirrhosis. In view of the history of alcohol consumption preceding the taking of cincophen the question arises as to which accounts for the pathologic changes.

At one time during the patient's stay in the hospital his cholemia was so marked and his condition so grave that the experimental omentopexy which was under consideration had to be postponed for ten days. During this time caffeine sodium benzoate by hypodermatic injection and by *paracentesis abdominis* were most effective in improving his condition. Two courses of salygen were without noticeable benefit.

When operation was performed the increase in size of the vessels of the round ligament indicated that nature was already attempting to bring about the collateral circulation sought artificially by the omentopexy.

Parental liver in the form of "extralin" was begun early and continued for several months after operation (given orally later) with good result. Dextrose was exhibited in dose of 2 to 3 oz. daily.

The abdomen was tapped once more after the patient returned home, following which the excessive peritoneal fluid gradually disappeared. At the same time the total urinary excretion rose to 100 to 130 oz. in 24 hours. This output has continued (90-100 oz. per 24 hours) up to the present time.

Our experience with this case convinces us that, in selected instances, it is of practical value to supplement the portal circulation by omentopexy. The support and stimulation of what normal liver tissue remains would seem to be accomplished best by liver extract and dextrose.

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NOTICE

The demand for back numbers of this journal has been so unexpectedly large that the publisher is left with only enough on hand to fill orders for bound volumes. To those subscribing to the Journal, it will be encouraging to learn that the publishers are considering planographing all previous issues into an inexpensive edition, provided sufficient demand continues to be evident.

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CONTENTS

SECTION I—CLINICAL MEDICINE — *Page*

SOME OBSERVATIONS UPON THE RECIPROCAL RELATIONSHIP BETWEEN GASTRO-INTESTINAL AND FEMALE PELVIC DISTURBANCES—*Julius Friedenwald, M.D. and Samuel Morrison, M.D.* — 609
DISCUSSION AND APPRAISAL OF SOME FUNCTIONAL DISTURBANCES OF THE DIGESTIVE TRACT—*H. F. Kramer, M. D.* — 614
ABSTRACTS — 617

SECTION II—EXPERIMENTAL PHYSIOLOGY

A COMPARISON OF METHODS FOR THE QUANTITATIVE ESTIMATION OF DIASTASE IN DUODENAL FLUID—*C. R. Schmidt, M.S., H. Greengard, M.S. and A. C. Ivy, Ph.D., M.D.* — 618
ABSTRACTS — 627

SECTION III—NUTRITION

THE COMPLETE TREATMENT OF PERNICIOUS ANEMIA—*Russell L. Haden, M.D.* — 628
ABSTRACTS — 634

SECTION V—THERAPEUTICS

TREATMENT OF FUNCTIONAL VOMITING—*C. H. Drenckhahn, M.D. and D. L. Wilbur, M.D.* — 635

SECTION VI—ABDOMINAL SURGERY

THE RELATION OF ANEMIA TO SURGICAL DISEASES OF THE GALL BLADDER—*Ralph A. Kordenat, M.D.* — 638
ABSTRACTS — 645

SECTION VIII—EDITORIAL

SHALL WE HAVE "STOMACH SPECIALISTS" OR INTERNISTS CERTIFIED AS GASTRO-ENTEROLOGISTS BY A QUALIFIED NATIONAL BOARD?— 646
PROPOSED CONSTITUTION AND BY-LAWS OF THE AMERICAN BOARD OF GASTRO-ENTEROLOGY — 649

SECTION X—AFTER "HOURS"

JEAN PAUL MARAT, M.D.—THE FRENCH PHYSICIAN-REVOLUTIONIST—*J. Duffy Hancock, M.D.* — 653

SECTION XI—SOCIETIES, PROGRAMS AND PROCEEDINGS

THE HISTORY OF THE NEW YORK GASTROENTEROLOGICAL ASSOCIATION—*Anthony Bassler, M.D.* — 667

SECTION XII—"THE CLINIC"

RECTO-SIGMOID CANCER WITH ACUTE GANGRENE OF PELVIC ORGANS—*Charles E. Howard, M.D., F.A.C.S.* — 669
AN INSTANCE OF UNCONTROLLABLE VOMITING OF LONG DURATION: ADVANCED MALNUTRITION: HYSTERIA: METAL POISONING: RECOVERY—*Frank Smithies, Sc.D., M.D.* — 671

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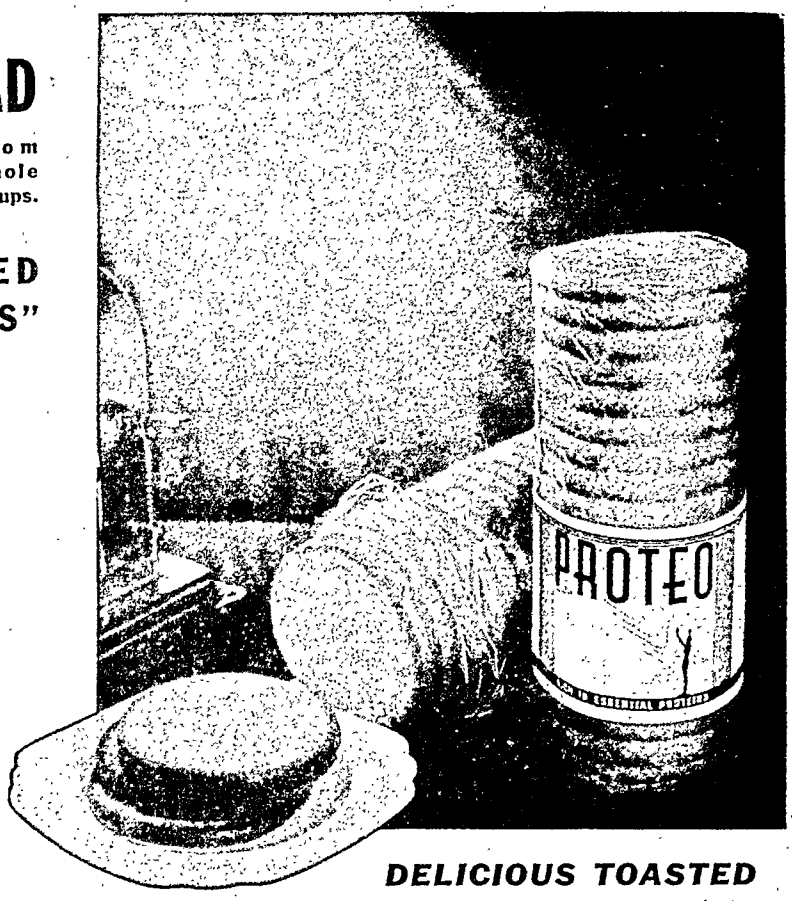
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Some Observations Upon the Reciprocal Relationship Between Gastro-Intestinal and Female Pelvic Disturbances*

By

JULIUS FRIEDENWALD, M.D.†

and

SAMUEL MORRISON, M.D.

BALTIMORE, MARYLAND

THE gastro-intestinal disorders incident to female pelvic disorders have by no means received the attention which their importance warrants. In a former communication we[1] attempted to point out the frequency and significance of gastric affections occurring at the menopause. It is our object in this paper to consider more fully the interrelation of gastro-intestinal affections and female pelvic disease.

For convenience these affections may be divided into two large groups:

A. GASTRO-INTESTINAL SYMPTOMS DUE TO FEMALE PELVIC DISEASE.

B. PELVIC DISTURBANCES RESULTING FROM GASTRO-INTESTINAL DISEASE.

A. GASTRO-INTESTINAL SYMPTOMS DUE TO FEMALE PELVIC DISEASE

It has long been recognized that pelvic disease is frequently the cause of gastro-intestinal symptoms. Andresen[2] called attention to this fact and observed that of 1,500 patients applying for gastro-intestinal symptoms 160 (17%) had female pelvic disorders as the sole or underlying cause of the symptoms and that the incidence of female pelvic disease as the cause of gastro-intestinal symptoms was 25%.

The mechanism by which these symptoms are made manifest may be explained by a disturbance arising in: (1) the *nervous system*, (general or reflex causes); (2) *the endocrines;* (3) the direct *contact caused by pressure* from affected female generative organs upon the digestive tract and (4) as the *result of infections and metastases* secondary to disease of the pelvic organs.

1. *The Nervous System:* Nervous manifestations in disturbances of the female organs are extremely common and occur in the form of neurasthenic, hysterical or psychasthenic symptoms. These may be accounted for mainly by a general weakness or depression of the nervous system appearing not only at puberty and during the menopause but frequently as the result of actual pelvic disease. The abnormal irritability and instability of the pelvic system unquestionably is a factor of great importance in the production of nervous manifestations, occurring not uncommonly on the distinct basis of a vagotonia.

Many of the disturbances likewise can be accounted for as reflex neuroses as the result of impulses passing through vagus and sympathetic paths. Wharton[3] has recently called attention to the fact that the pelvic organs derive their immediate nerve supply from the abdominal sympathetics. He points out that since this is likewise the source of the intestinal nerve supply, therefore, it may account for the occurrence of reflex gastro-intestinal symptoms in disease of the female generative organs. In his beautifully demonstrated anatomical dissections made from the study of human cadavers, the interrelationship of autonomic nerve fibers between the pelvic organs and the digestive system is clearly defined. A clinical example of this close connection is observed in the many gynecological cases in which pain is referred entirely to the rectum. Moreover, abdominal distention and other chronic gastro-intestinal symptoms have not infrequently been observed as accompaniments of pelvic diseases which, according to Wharton, may be explained on the basis of the close neurological relationship between these organs.

In this connection it is interesting to note that Zondek[4] has called attention to the instability of vascular innervation at the menopause. This theory likewise may explain how paroxysmal

*From the Gastro-Intestinal Clinic of the Department of Medicine, University of Maryland, Baltimore.
Read by title before the Association of American Physicians' Forty-ninth Annual Meeting, Atlantic City, May 1 and 2, 1934.
†Professor of Medicine (Gastro-Intestinal Diseases), School of Medicine, University of Maryland.
Submitted July 27, 1934.

shiftings of the blood to and from the abdominal and pelvic organs may account for symptoms referable to the gastro-intestinal tract in pelvic disease. From these observations it is, therefore, not difficult to understand the frequency with which nervous gastro-intestinal manifestations occur in pelvic disease.

The gastro-intestinal symptoms more frequently observed are fullness, distention, eructation of the aerophagic type, acid belching, regurgitation, epigastric distress and pain, nausea and vomiting. Anorexia is frequent though periods in which increased or perverted appetite occur are not unusual. Symptoms of hyperchlorhydria often alternate with those of achlorhydria. The symptoms vary markedly in severity, alternating often with periods of relief which periods are not especially influenced by the character and quantity of food taken. Often they are associated with general nervous symptoms such as globus hystericus, insomnia, headaches, lassitude, instability and depression and are not uncommonly increased by anxiety and sorrow.

The gastro-intestinal manifestations may become so unusually prominent as to overshadow those due to the actual, primary pelvic disorder which may be overlooked unless the possibility of the presence of such an affection be held in mind and an investigation as to its presence be undertaken.

The diagnosis must be based on the nervous type of the digestive symptoms, the occurrence of pelvic signs and finally upon the demonstration of the presence of a definite pelvic lesion. Obviously the gastro-intestinal symptoms should disappear following the correction of the pelvic disturbance. The following history briefly represents an instance of this condition:

A. M., aged 49 years, had always enjoyed good health until three years ago, when symptoms incident to the menopause first were noted. These consisted of an irregularity in the menstrual periods, sometimes profuse, at others scant, with pelvic pain and nervous gastro-intestinal symptoms taking the form of increasing constipation, nausea, anorexia and abdominal distention, heartburn and eructations, insomnia, depression and headaches. There were many periods in which the patient appeared quite well but during the past year these have become far less frequent. The condition was dismissed by her physician as "nothing unusual", "incident to the menopause", and the patient was advised to rest at the sea-shore. Not improving, however, she returned for a more complete investigation. The patient had lost 15 pounds in weight during the past year; she was weak and easily exhausted. The symptoms already noted were more intense and continuous.

On physical examination the abdomen was found soft and relaxed and in its lower area a hard mass could be detected, evidently arising from the pelvis. The Ewald test meal revealed a hyperchlorhydria. The stool contained considerable mucus but was otherwise normal. A gastro-intestinal *roentgen-ray series* revealed a spastic gastro-intestinal tract together with a maximum prolapse. *On pelvic examination* a large fibroid tumor pressing upon the rectum and extending out of the pelvis into the abdomen was found. *At the operation*, (a hysterectomy was performed), this condition was verified. No other abnormalities were detected within the abdomen. The patient made a speedy and uneventful recovery with a prompt disappearance of the digestive symptoms.

2. *Endocrine Dysfunction:* Frequently gastro-intestinal symptoms occur as the result of endocrine dysfunction due to disease of the pelvic organs. These manifestations are noted at the menopause but are quite as common with pelvic disease due not only to ovarian insufficiency but also to multiglandular disturbances associated with ovarian dysfunction. The thyroid, pituitary and adrenal glands in addition to the ovary may be involved in this endocrine dysfunction.

The gastro-intestinal symptoms manifested are often indefinite, vague and extremely variable, largely dependent upon the type of gland most prominently involved. They occur as diarrhea or constipation, eructations, loss of appetite, nausea, vomiting, fullness and distention following meals, associated with hot flushes, sweats, palpitation, vertigo, faintness and extreme nervousness. In some instances there is an excessive gain in flesh but in others the reverse occurs.

The diagnosis may become extremely complicated and uncertain. It must depend in addition to the information given by the general symptoms, largely upon the demonstration of a glandular dysfunction in a patient presenting marked digestive symptoms with pelvic disease.

An instance of glandular dysfunction associated with pelvic disease is briefly presented in the following interesting case of "gastro-intestinal hyperthyroidism":

P. F., aged 48 years, had enjoyed good health until 2½ years ago when, following financial reverses, she began to suffer with nervous depression, weakness, palpitation and indigestion and complained of pain in the lower abdomen, loss of appetite, constipation alternating with attacks of diarrhea, nausea and occasional vomiting. The menstrual periods which had previously been irregular had entirely disappeared two years ago. The patient had lost 20 pounds in weight.

On physical examination, the thyroid was not palpable. The heart was rapid but was otherwise normal, pulse 114, blood pressure 138/80. The abdomen was soft and relaxed. There was marked tenderness in both the right and left sides in the lower abdomen. *An Ewald test breakfast* revealed a normal acidity. The *basal metabolic rate was plus 36*. A gastro-intestinal *roentgen-ray series* revealed a spastic gastro-intestinal tract. A *pelvic examination* showed the presence of bilateral ovarian cysts.

The diagnosis of masked hyperthyroidism with gastro-intestinal involvement and ovarian disease was made. Following two weeks of rest and symptomatic treatment of the digestive tract and nervous system with the addition of Lugol's solution in a moderate dosage for short periods, the patient improved sufficiently to warrant the risk of an *abdominal operation*. This was performed; a large right ovarian dermoid cyst and a somewhat smaller left one were removed. The patient made an uneventful recovery, gained flesh rapidly with a prompt disappearance of the digestive and nervous symptoms. The basal rate gradually fell to normal.

3. *Direct Contact of the Affected Generative Organs:* Disturbances of various forms associated with the generative organs producing pressure upon the gastro-intestinal tract may play an important role in the production of digestive symptoms. These may occur as the result of pres-

sure or retroflexion, retroversion or enlargement of the uterus or may be due to tumors or as will be further elaborated later, to chronic inflammatory changes. As a result, gastro-intestinal symptoms of a more or less severe type may be produced. At times there may even be evidences of obstruction. It may, however, be of interest to note in this connection, that instances of retroversion are not uncommonly observed associated with enteroptosis in which both the digestive as well as the uterine symptoms equally arise as the result of a common cause, namely a general visceroptotic state.

Among the affections directly concerned with the generative organs producing digestive symptoms as the result of pressure may be mentioned pelvic tumors of various forms as uterine fibroids, malignant growths of the uterus and the adnexa, ovarian tumors and cysts, inflammatory enlargements of the uterus, salpingitis, extra-uterine pregnancy and ascites due to malignancy of the pelvic organs. The result of such pressure is manifested largely in an interference with the motility of the bowel leading from the mildest types of constipation to partial or even to complete obstruction. In addition, as the result of pressure from direct contact, inflammatory changes such as gastritis, colitis (mucous and spastic), proctitis and hemorrhoids may occur in the gastro-intestinal tract itself.

The gastro-intestinal symptoms most commonly observed are abdominal pressure, pain, enlargement, distention, nausea, vomiting, eructations, heartburn, increasing constipation often alternating with brief attacks of diarrhea. These symptoms are frequently indicative of the presence of a partial obstruction of the bowel and become more and more intense as the tendency to complete obstruction increases.

The diagnosis is not usually difficult. The presence of the abdominal enlargement together with a tendency to increasing constipation and partial obstruction will indicate the need of a complete investigation. A pelvic examination will ordinarily reveal the correct diagnosis. Occasionally the gastro-intestinal symptoms may be so prominent as to overshadow those due to the pelvic disease.

In the *differential diagnosis*, it is important to determine whether one is actually dealing with a primary gastro-intestinal affection or a secondary involvement from the pelvis. For example, an acute intestinal obstruction has been mistaken for a twisted ovarian cyst, a chronic appendicitis for ovarian disease and carcinoma of the pelvic colon for obstruction produced by a fibroid tumor, etc.

In addition to the pelvic examination, a gastro-intestinal roentgen-ray investigation may be of great aid in the diagnosis. The barium enema is often especially helpful in this regard.

As an illustration of the effect of pressure upon the digestive tract due to the pelvic organs we need only recall cases familiar to all in which digestive symptoms of various kinds present for long periods have entirely disappeared following suspensions of the uterus.

The following case history presents an instance in which gastro-intestinal symptoms were due to pelvic disease:

The patient, L. M., aged 45, complained of a variety of dyspeptic symptoms for the past year. She suffered with abdominal fulness and distention, slight nausea, heartburn, eructation, occasional pain and constipation. At first these symptoms were insignificant with occasional periods of relief extending over several weeks. The discomfort was apparently related to the diet as it occurred even with the simplest food. There was but a slight loss in weight. The periods had become irregular and occasionally were extremely profuse. With the impression that the symptoms were largely produced by the menopause almost a year elapsed before the patient submitted to medical advice and then only because of the increasing constipation inasmuch as the usual laxatives no longer produced their desired effect.

On examination the abdomen was found extremely relaxed, somewhat distended and tender in its lower quadrants. A smooth hard mass arising from the pelvis could easily be palpated extending almost halfway to the umbilicus. *A pelvic examination* revealed the presence of a large uterine fibroid impinging firmly upon the bowel. A complete physical and laboratory investigation revealed no further abnormalities and operation was advised. A hysterectomy was performed with entire relief from all the gastro-intestinal symptoms.

4. *Infections and Metastases:* It is well recognized that certain inflammatory and purulent pelvic processes acting as primary foci of infection as well as metastases from malignant disease of the uterus or ovaries may give rise to digestive disturbances of greater severity at times than those manifested by the primary disease. Andresen[4] points out that lesions such as peptic ulcer, cholecystitis and appendicitis may originate from such causes as focal infections; 60% of his cases were of this type. We have likewise observed this relationship in our cases as not unusual and have been impressed with the fact that these types of focal infection have not generally received the recognition that their importance warrants.

Focal infections may arise from the tubes, ovaries and uterus. The following history briefly presents a case of this type:

K. M., aged 29, presented definite evidences of recurrent duodenal ulceration over five years with many periods of entire subsidence and apparent cure. An attempt was made to determine a source of infection but none could be found until a chronic purulent salpingitis was detected which had been present for many years and known to the patient but not divulged.

Metastases from pelvic growths to the stomach are not common except in the case of that little understood Krukenburg tumor which will be discussed later. Pelvic growths may affect the gastro-intestinal tract by direct extension.

Attention should also be directed to certain more or less physiological disturbances with reciprocal effects on the two systems under discussion. For example, according to Walschied[5] it may be shown, in general, that menorrhagia diminishes gastric secretion even to an achlorhydria, while the opposite state may cause hyper-

chlorhydria. This phase will be discussed further subsequently.

B. PELVIC DISTURBANCES SECONDARY TO GASTRO-INTESTINAL DISEASE

While pelvic disturbances resulting from disease of the digestive tract are by no means as common as dyspeptic symptoms due to female generative disease, their importance nevertheless requires careful consideration. These reciprocal effects may occur: (1) As the result of nervous manifestations; (2) As the result of inflammatory lesions in the digestive tract; (3) As the result of tumors involving the digestive tract; (4) As a result of gastric-secretory disturbances.

1. *Nervous Manifestations:* Nervous digestive manifestations are known to influence puberty, the menstrual cycle, and the menopause in various ways. The symptoms most frequently complained of are general nervous manifestations such as irritability, depression, insomnia, headaches and malaise, all referred to the pelvic organs in some way and associated with such nervous digestive symptoms as nausea, vomiting, abdominal pain, discomfort, distention and eructations.

2. *Inflammatory Lesions Involving the Digestive Tract:* The close relation existing between the digestive and female generative organs frequently give rise to difficulties in diagnosis. This is especially manifested in those instances in which inflammatory processes occur in organs which are adjacent and in which it may become difficult and at times impossible therefore to determine the primary seat of the lesion. The appendix is of especial interest in the female on this account since, for instance, ovarian and tubal disease are frequently mistaken for appendicitis and vice versa. It has long been recognized that a definite connection exists between appendicitis and disturbances of menstruation and often severe dysmenorrhea may be confused with appendicitis. In this connection it may be well to call attention to the fact that exacerbations of an acute attack of appendicitis are not uncommonly observed during the menstrual period. Hale[6] has pointed out that chronic appendicitis is often associated with a tender enlargement of the right ovary, cystic in type, and concludes that chronic appendicitis produces a deleterious effect upon the right ovary and on this account advises early removal of the diseased appendix. Of 250 cases of chronic appendicitis 76% were found at operation to be associated with the small cystic ovary just described. Dencks[7] and others likewise remark that even though the appendix may be found normal at operation it should be removed due to the fact that inflammatory changes may be produced later as the result of lesions occurring in the adnexia. On the other hand, it is important to remember that following purulent inflammatory changes in the appendix the pelvis not uncommonly becomes involved and consequently there follows chronic inflammatory changes, adhesions, and fixation of the uterus.

Similarly, inflammatory affections of the descending colon, sigmoid and lower bowel in the form of a colitis, sigmoiditis or proctitis may by direct contact as well as by extension of the process produce changes in the surrounding pelvic organs leading to pelvic adhesions.

3. *Tumors Involving the Digestive Tract:* These may produce their effect either by direct contact or as the result of metastases to the pelvic organs. There is in addition to the usual form a type of malignant growth known as the "Krukenburg tumor" (to be discussed in more detail) which secondarily involves the female generative organs and which in recent years has assumed an increasing interest.

Of the malignant growths of the digestive tract secondarily involving the female generative organs numerous instances have been recorded, occurring both as the result of metastases and extension or direct contact. The pelvic organs may be involved in a generalized carcinomatosis. Roblee[8] reports an interesting case of secondary adenocarcinoma of the ovaries due to annular adenocarcinoma of the jejunum with metastatic lesions in both ovaries. Cases of carcinoma of the colon with involvement of the pelvic organs are extremely common. These occur especially with cancer of the pelvic colon and rectum. Dupont and Lievre[9] report an instance of cancer of the stomach with metastases to the ovary and sacrum. Goinan and Montpellier[10] report a colloid epithelioma of the rectum with ovarian metastases in a female aged 20 years and Horning,[11] an instance of a tumor of the left and right ovaries in a female aged 41 with a metastatic involvement of a large part of the colon and lower ileum due to a primary cancer of the appendix.

A less common type of secondary malignant involvement of the ovaries is observed in the so-called "Krukenburg" tumor. Hundley[12] has collected 102 cases in which this form of tumor was found. He points out that while a primary carcinoma rarely develops in an organ in which metastatic cancer commonly occurs and *vice versa*, the ovary is, however, an exception to this rule and may be the seat of both primary and secondary growths.

Secondary ovarian malignant tumors of the Krukenburg type occur as metastatic growths from primary involvement of the stomach, small intestine (jejunum), large intestine (sigmoid and rectum), gall bladder and appendix. The stomach is most frequently the seat of the primary growth but invasion into the ovaries, intestine and peritoneum is an early manifestation. The ovarian involvement is usually bilateral. Occasionally metastases take place into the breasts as was noted by Chevalier Jackson and W. Wayne Babcock.[13] When the stomach is primarily involved the symptoms are those usually noted in gastric malignancy, that is, distention, nausea,

vomiting, anorexia and loss of flesh. Abdominal pain is not unusual; ordinarily it is most prominent in the epigastrium and in the left hypochondrium appearing often one to two hours after meals with relief following vomiting. Occasionally gastric hemorrhage occurs as was observed by Cain[14] in his case in which two hemorrhages were noted, one of which was extremely severe. Constipation is usual.

The abdomen is usually found distended with a shifting dullness indicating the presence of free abdominal fluid. The gastric acidity is low and achylia gastrica is usually present. The roentgen-ray examination ordinarily presents the picture observed in linitis plastica, that is, a small, contracted stomach. When the intestines are involved signs of obstruction are noted which can likewise be detected by means of roentgen-ray examination.

While the gastric symptoms usually are prominent they may be so slight as not to be recognized during life. The pelvic symptoms may likewise be more or less distinctive; most frequently dysmenorrhea is observed, occasionally menorrhagia or metrorrhagia. Pelvic examination will usually reveal the ovarian tumors which are ordinarily bilateral.

At operation or autopsy the organs involved in the carcinoma contain the characteristic mucoid degenerated and signet ring cells of the Krukenburg type. These are not only observed in the primary growth which is usually in the stomach but likewise in all metastatic involvements. The ovaries present a general enlargement, retaining their usual form with a smooth surface, free from adhesions. The signet cell is the definite pathognomic sign of the Krukenburg tumor and may be observed both in the medullary and scirrhus types.

While the usual metastases to the ovary occur by way of the lymphatics, by direct extension and contact or through the blood stream, the Krukenburg tumor according to Hundley is metastasized by the lympatic route from the stomach to the lumbar glands by way of the subpyloric plexus. It appears quite probable that the primary gastric lesion observed so frequently associated with Krukenburg ovarian tumors is identical with the so-called carcinoma plastica or the more generally known linitis plastica. However, linitis plastica occurs in both sexes, whereas, Krukenburg tumors occur only in the female.

4. *Gastric Secretory Disturbances:* In certain instances of achylia anemias occur. Strauss and Castle[15] have called attention to changes in gastric acidity associated with the anemias of pregnancy. In the "physiological anemias" of pregnancy there is a reduction in the gastric acidity; on the other hand, in the hemolytic anemias of pregnancy which resemble pernicious anemia, achylia is a prominent pathogenic feature and from our knowledge of the etiologic factors concerned in pernicious anemia it is logical to assume that the gastric secretory disturbance plays some significant role in the anemia associated with pregnancy.

Likewise there are certain anemias of the hypochromic type which respond more specifically to the administration of iron that are associated with an achlorhydria and its accompanying symptoms. This form of anemia is frequently observed at the menopause and is possibly associated with a pelvic dysfunction.

Van Derhoof and Davis[16] recently reported five cases, all women (ages 37 to 46), of microcytic anemia associated with atrophic glossitis, achlorhydria and increased blood loss at the menstrual periods. When the treatment, which consisted of large doses of iron, and adequate amounts of hydrochloric acid, was omitted the anemia recurred. They reported that hysterectomy may be advisable to prevent the periodic blood loss. Hurst[17] also called attention to the simple achlorhydric anemia which occurs almost exclusively in women and in the development of which menorrhagia is often a contributory factor. Haden and Singleton[18] as well as others consider this type of anemia as a deficiency disease principally because it responds readily to adequate doses of iron. They remark especially upon the frequency of abnormalities of menstruation and view the latter as one of the most characteristic features of simple achlorhydric anemia. In all cases of unexplained menstrual disturbances they suspect simple achlorhydric anemia and proceed to verify or exclude their suspicion by gastric analysis and careful blood examination.

CONCLUSIONS

1. An intimate relationship exists between disturbances of the digestive and female generative organs.

2. Attention has been drawn to the fact that the gastro-intestinal symptoms due to pelvic disease are extremely common. This should be borne in mind inasmuch as those due to the digestive tract may predominate to such a degree that the primary pelvic disease may be overlooked.

3. On the other hand, pelvic disturbances may likewise occur as the result of gastro-intestinal affections. These are by no means so common nor as clearly understood but their importance warrants their further careful consideration.

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Discussion and Appraisal of Some Functional Disturbances of the Digestive Tract

By

H. F. KRAMER, M.D.
BROOKLYN, NEW YORK

THE unfortunate who suffers from indigestion, and who on account of his unstable emotional make-up has been labeled "neurasthenic" or "neurotic" experiences great difficulty in gaining the ear of a sympathetic physician. To most laymen the words neurotic or neurasthenic are synonymous with malingering; of course this is not true. To visit a doctor and describe symptoms of abnormal type is not an indication of normal health. The individual would seem mentally to be sick if no organic basis can be found sufficiently adequate to account for his trouble. Patients in this class need to be defended, for, when they are analyzed, often it is found that a large proportion exhibit, as Alvarez has pointed out, family psychic instability while, in others, some real defect in the alimentary tract (it may be functional or organic) accounts for their complaints.

The functional aberration uncovered during a careful gastro-intestinal survey usually is one affecting the smooth muscle coats of the digestive tube—motor imbalance. The rhythmic contraction of these muscle fibres so can be altered that a numerous variety of gastro-intestinal symptoms result and organic disease closely simulated. Disturbances of secretory function usually are an accompaniment; in themselves seldom are they productive of physical discomfort.

In general the presenting symptoms vary with the part of the digestive tube in which the normal muscular behavior is changed and with the character and degree of that change. There may be spasms of segments of the digestive tube of greater or lesser extent, reversal of peristalsis or absence of peristalsis. When the patient complains of "lump in the throat" or difficulty in swallowing all or part of the oesophagus is in spasm. A complaint of pressure or fullness in the epigastrium may mean spasm of the cardia or the pylorus. Regurgitation, heartburn or sour eructation may indicate reverse peristalsis sufficient to force a portion of the stomach contents into the oesophagus. The common symptoms, "gas" and belching, may be explained on the same basis. "Gas in the stomach" almost always is swallowed air; these patients find by experience that swallowing air and later belching it will relax the contracted segment of smooth muscle causing distress. Thus logically they assume that having obtained relief by belching it that the gas is the offending agent. (1)

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Regurgitation is distinguished from vomiting in that it is often voluntary, is not associated with nausea or salivation and that only a mouthful is brought up at a time. The repeated regurgitation of gastric contents into the lower oesophagus may be responsible for an oesophagitis which in turn gives rise to heartburn; such pyrosis is not, as commonly supposed, dependent upon increased acidity of the gastric contents.

Spasm severe enough to cause a "drag" upon the peritoneum will cause sharp pain. It has been shown that the abdominal viscera do not contain pain-sense nerves but that the peritoneum does. (2)

Uncorrelated spasm of unrelated segments of the lower intestinal tract ("spastic colitis" commonly associated with constipation) often is seen in patients under emotional stress. Such condition is favored by the habit of eliminating one food after another from the diet and the tendency thus to subsist on a low residue food intake. The symptoms complained of are abdominal pains and cramps accompanied by constipation. Spasm is produced by overstimulation of the motor fibres of the sympathetic nerves to the gut. At times disturbance of the peristaltic gradient may cause increased peristalsis and diarrhoea then occurs. (3)

The common causes of functional disturbance of the gastro-intestinal tract are:

(1) Emotional upsets; (2) Failure to lead a physiological life; (3) Allergic responses; (4) Mechanical faults.

First let us consider functional disturbances of the alimentary canal which are due to emotional conflicts and complexes and their different reactions. Practically in my work I have learned that tactful questioning can bring out that the mental distress and its consequences may be attributed usually to one of four causes: Grief or sorrow over death of friend or relative; worry or fear—usually of financial loss; constant bickering in the home or domestic unhappiness; sexual maladjustment.

I am aware that psychologists recognize a more complete list of primary emotions. Sadler enumerates the following: (4) Fear, disgust, wonder, elation, subjection, tenderness, sex hunger, food hunger, security, hoarding, pride of creation, anger.

According to this author these are combined to form fifteen secondary emotions and these again

combined to make ten "sentiments". The sentiments are again compounded to produce seven "controlling convictions". These are the complicated tools of the psychoanalyst and really have no place in practical gastro-enterologic diagnosis. However, knowledge of the possible digestive anomalies dependent upon the complex interplay of the emotions is essential to a proper understanding of the symptomatology capable of being caused by anomalies of the psyche as distinguished from those due to organic or secretory faults.

The first interview with the patient is helpful in placing him in a proper category. The pure "neuro" or the case which is predominantly psycho-neurological may be exemplified by the well-to-do woman who delights in visiting the doctor. She prances in talking volubly and does not listen to what the physician may say. Again the truculent man, demanding in his manner, states his diagnosis, what he wants done about it and may end up by maligning his last medical advisor: when pressed for a chief complaint, he may be stumped for a moment and then reply with a question such as "should these veins in my hand be flat?", or "do you call mine a healthy complexion?" Unless some definite digestive symptom can be elicited patients of this type immediately should be referred to a psychiatrist. Usually they will not submit to an orderly gastro-enterologic survey anyway; nearly all will balk at the suggestion that a test-meal be removed by the stomach tube.

The patient whose digestive system really is upset on account of a true nervous condition will enter with a sullen or distrustful air if previously he has been rebuffed, or with a worried expression, watching narrowly for any sign of disinterest or impatience on the part of the physician. Then follows a list of doctors whom he has seen and the diagnoses which have been made; perhaps a detailed enumeration of the articles eaten in the past few days. The picture is a familiar one. The impatient physician may decide at that point that further investigation is not worth while and say, "the trouble is all nervous"; or assume the accusatory attitude with the statement, "you have started all this trouble in your own mind—you will have to get yourself out of it". If this occurs in either case, here his usefulness to that patient has ended. The physician who will listen seriously, extending just enough interest and sympathy when necessary and who, without committing himself, then will begin a thorough examination, has more chance of succeeding. Gastro-enterologists have been criticized for putting these patients through a routine alimentary tract survey, but this very examination apart from eliminating possible organic disease and disclosing many of the functional irregularities which may cause the symptoms, really is the beginning of the treatment of that patient. Now he is satisfied that at last an earnest effort is being made to find his trouble. His story has not been thrust aside as silly, and if nothing abnormal is found, this observation can be presented to him gradually and more convincingly, while if something tangible and treatable has been discovered this fact will engender a sense of relief and a more co-operative spirit.

One is always anxious until organic disease thoroughly has been ruled out for not rarely among so-called "neuros" there may be discovered incipient tuberculosis, hyperthyroidism or even early cancer of the stomach or bowel.

General treatment should be directed towards retarding the pace of living. If a leisurely vacation is not possible, shorter hours of work, rest before and after meals, avoidance of eating when tired or angry, excited or otherwise emotionally upset, will relax smooth muscle. Small feedings of high caloric value at frequent intervals will improve nutrition.

The patient should be taken into the doctor's confidence and explanation made how mental irritation can cause the functional disturbance of digestion. Then any local defect which has been found can be treated; the oesophageal spasm by lavage or dilatation if necessary; the spastic bowel with abdominal compresses (cold cloths covered with an impervious dressing and worn over night), tonics, and moderately bulky diet; abdominal exercise and massage in the atonic cases; drugs as antispasmodics such as bromide and atropine, luminal and other barbital compounds: hyoscyamus, lupulin, cannabis indica and extract of sumbul, all have their advocates.

Another group of patients affected with functional dyspepsia are ill from a failure to lead a physiological digestive life. Overeating may cause overcrowding of the stomach, the intestines and liver with consequent symptoms. If the insult is not too often repeated it will subside upon a regime of fasting and with appropriate catharsis.

Tobacco has been shown to produce pylorospasm and a pain-cycle simulating that of peptic ulcer. Overwork, inefficient mastication, lack of exercise and the occurrence of constipation need no further mention.

Gastro-intestinal allergy may cause many symptoms and simulate many organic diseases. Although allergy may not come properly under the head of functional disturbance, many patients suffering from it and its consequences are classed as neurotics before the true state of affairs is discovered or even suspected. Dr. A. H. Rowe in his recent book, "Food Allergy", bases the diagnosis on the following data:

1. The presence of an allergic tendency in the patient or his relatives. A family history of chronic indigestion is often due to inherited food allergy especially where other manifestations, such as migraine, urticaria or asthma are present in the patient or his relatives.

2. The history of definite food idiosyncrasies or dislikes.
3. The presence of skin reactions to foods. Among the common complaints occurring are canker sores in the mouth, coated tongue, heavy breath, distention, belching, burning, nausea, vomiting, mucous colitis, diarrhoea, proctitis, pruritis ani and pain and soreness in almost any part of the abdomen. Acute attacks have been operated upon for appendicitis, for besides the local manifestations such patients may even have fever and leucocytosis.

Treatment, when allergy is the basis of the digestive disturbance, depends on the elimination of the foods to which mild or severe sensitization exists. This is said to be possible of accomplishment by means of Rowe's elimination diets which contain foods to which patients infrequently are sensitive.

Certain mechanical conditions, particularly duodenal stases, often cause digestive symptoms; physical findings may be vague and for this reason the patient often is classed as neurotic. One of the most important of these mechanical conditions, and one which should be more carefully searched for, is chronic duodenal stasis (5) and (6). This condition best is diagnosed with the aid of the fluoroscope. Radiographs taken in the face-down position do not easily show it because this position favors release of the obstruction. On the fluoroscopic screen the duodenum fills as soon as the pylorus relaxes a little at times and thus demonstrates actual duodenal dilatation; then the barium progresses to the jejunal angle only to surge backward again. The duodenum may be seen to writhe or labor over contents in excess of normal; such condition may be associated with cramp-like pains. If positive signs should be exhibited by the radiograph they are "puddling" or delayed emptying of the duodenum, usually with accompanying dilatation.

Chronic duodenal stasis also may be due to extrinsic causes such as gastroptosis, peritoneal bands or external pressure from tumors or as a result of inflammatory conditions. Gastroptosis acts by increasing the acuteness of the superior duodenal angle or by compression at the mesenteric root. It is possible that many of the vague symptoms of gall bladder disease between acute colic attacks are due to the periduodenitis which accompanies it and thus causing duodenal stasis.

Bands and membranes are developmental or inflammatory. As a result of non-absorption of embryonal folds the lesser omentum may extend to cover the gall bladder or downward to the colon, forming the hepatoduodeno-colic ligament. (Bryant, Smithies.) Many writers on the subject believe that this ligament when attached to a low, full caecum will exert a drag which supplies the necessary compression where the ligament crosses the duodenum. Kantor (7) finds that hyperdescent of the caecum commonly accompanies duodenal stasis.

An understanding of the developmental anomalies of the duodenal tube involves a knowledge of the embryonal development of the alimentary canal from its withdrawal from the vitelline vesicle to the rotation of the colon and the duodenum.

Symptoms occur when the peristaltic efficiency is insufficient to overcome the obstruction. The balance may be slowly lost with gradually increasing symptomatology. It may be lost suddenly; in such circumstances symptoms are apt to be acute.

The symptomatology of duodenal stasis variously is described by different authors so that there is no clear-cut clinical picture. The symptoms most often mentioned are nausea, regurgitation, weakness, headache, mental and physical depression, disturbed heart action, faintness and cold extremities. The toxins described as forming in the duodenum with obstruction undoubtedly are responsible for some of these symptoms. This, the reader will recognize, is exactly the picture described for digestive disturbances due to so-called neurasthenia.

Whitachre (8) says: "An unmistakable group of symptoms cannot be defined, yet I am of the opinion that in the absence of positive findings for ulcer, cancer, gall bladder or kidney the following symptoms indicate chronic duodenal obstruction: Loss of appetite, gas distension and pain in the upper abdomen; an early feeling of fullness at meals; a gradual reduction in articles and amount of food taken; periodic attacks of vomiting or bilious attacks; loss in strength and weight; neurasthenia; dizziness; malaise." In treatment, rest in bed after meals is beneficial. Duodenal enlargement not always is demonstrable by X-ray studies.

According to Kellogg (6), when duodenal stasis is present, two areas of discomfort commonly are observed: at the left of the median line slightly above the navel and above to the right of the navel extending under the liver and to the shoulder. This distress may be a painful colic, intense and boring in character due to peristaltic unrest, or a steady dull ache, due to distention, often lasting until it is relieved by vomiting. Occasionally, pain is limited to the back between the shoulders. The discomfort may be relieved by deep pressure below the navel or by lying face downward with the fists pressed into the abdomen.

Treatment: The majority of cases of duodenal stasis is amenable to such treatment as is given for enteroptosis and intestinal stasis. Surgery is indicated when medical treatment fails or when the duodenum is greatly dilated. The surgical procedure varies with the conditions found at laparotomy and may be duodeno-jejunostomy with or without some plastic operation, gastro-enterostomy or severance of bands. Jennings has re-

lieved certain patients simply by dividing the ligament of Treitz.

According to Whipple, of New York, the treatment of this condition should be carried on by close co-operation among the gastro-enterologist, the psychiatrist and the surgeon.

High caloric feeding, abdominal support, lying prone after meals, occasional lavage and the mental guidance of the psychiatrist should be instituted until it has been proven that surgery is necessary to relieve the obstruction.

CONCLUSION

A routine study of the functions of the digestive tract will define more clearly the causes of the multiple and vague complaints which patients, unjustly accused of being neurotic, unfold, and will help to clarify the confusion of mind which most physicians bring to treatment. If this is done then there will be less need of the sign which Alvarez (9) has suggested for the waiting room of the intolerant physician:

"Nervous patients need not apply here because they will receive neither courtesy, proper attention, nor help."

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ABSTRACTS

BRET RATNER AND H. L. GRUEL.

Passage of Native Proteins Through the Normal Gastro-Intestinal Wall. Jour. Clin. and Invest. XIII. July, 1934 (517-532).

Since it is generally believed that under physiologic conditions, unsplit protein antigens are not absorbed through the intestinal wall, the authors determined to test the validity of such a concept by carefully conducted and controlled experiments on both animals and humans.

A perusal of the results obtained in both immature and mature guinea pigs leaves little room for doubt that oral sensitization can be produced in as high as 50 per cent of subjects. An interesting corollary was established by the observation that "shock" could result from a single feeding of the same protein that previously had been injected to establish sensitivity. This demonstrated not only the absorption of unsplit protein, but also its dramatic swiftness. A third interesting group showed that milder degrees of shock could be produced by ("shock") feeding animals previously sensitized solely via the alimentary route. The significance of this certainly is to be appreciated by those who have dealt with allergic gastro-enterocolopathies.

By means of the Prausnitz-Küstner skin phenomenon, a group of medical students demonstrated sensitivity to an orally administered antigen (cotton seed oil) not common to their diet. Many like experiments on a group of children showed similar results. Not only the mechanism whereby unsplit proteins are able to enter the blood stream directly, but also the defense whereby the body is enabled to survive the ingestion of new and strange protein foods is discussed. Absorption of unsplit proteins takes place by virtue of solubility and rapid passage through the pylorus. Furthermore, not all proteins are readily digested. Defensive resistance, on the other hand, is lent by the enzymatic digestion of protein, by the general impermeability of the intestine, by the development of specific anti-bodies, and by the renal excretory mechanism.

It is felt that lesions of the gastro-intestinal tract can alter permeability to such an extent that sensitization can take place, and finally that a limited normal absorption of unchanged proteins exists to protect against sensitization to the habitual protein of the diet.

H. J. Wolff, Rochester, Minnesota.

R. G. SINCLAIR.

Physiological Reviews. The Physiology of the Phospholipids. 14:351-403, July, 1934.

In an extensive review of the phospholipids, Sinclair points out that unlike the neutral fat of the body which is clearly a fuel substance and therefore shows wide variation in amount, the phospholipids are to be looked upon as an essential component of every tissue cell and like the proteins, water, and salts are relatively constant in amount, regardless of the nutritive state of the animal.

In regard to their function, the possibilities include: (1) that they are intermediary products in fat metabolism, (2) that they act as oxygen transport agents within the cells, and (3) that they are concerned in some more strictly physiochemical sense in the structural make-up and activity of the cell.

While the first of these three theories has enjoyed the greatest popularity and is still most widely accepted, Sinclair points out many well-established facts, all indicating that these substances fulfill some function other than that of intermediaries in the metabolism of fat.

Dwight L. Wilbur, Rochester, Minnesota.

ROGER M. HERRIOT AND JOHN H. NORTHRUP.

Crystalline Acetyl Derivatives of Pepsin. Jour. Gen. Physiol., 18:35-67, September 20, 1934.

In a broad attempt to determine the molecular structure of pepsin, Herriot and Northrup studied the effect on its activity of acetylation of various groups of pepsin. Three acetyl derivatives were isolated and obtained in crystalline form. The studies of these products show that acetylation of three or four of the primary amino groups of pepsin causes no change in the specific activity of the enzyme but that the introduction of acetyl groups in other parts of the molecule results in a marked loss of activity.

Dwight L. Wilbur, Rochester, Minnesota.

A Comparison of Methods for the Quantitative Estimation of Diastase in Duodenal Fluid*

By

C. R. SCHMIDT, M.S., H. GREENGARD, M.S.

and

A. C. IVY, Ph.D., M.D.

CHICAGO, ILLINOIS

IN SELECTING a method for measuring the diastatic activity of duodenal drainage, it was sought to determine which of several methods was best adapted for general use. The methods were: the Wohlgemuth method (1), McClure's modified Folin-Wu sugar determination (2), Leuders' Benedict reducing sugar determination (3), Willstätter's hypoiodite titration (4), and the Meyers-Bailey picric acid method (5).

In the past we have used the Wohlgemuth method for determining amylolytic activity in duodenal drainage. The method is based upon the production of erythrodextrin in a starch solution, the presence of the latter being determined by the color produced on the addition of a solution of iodine. The method has been subjected to severe criticism on the basis of time and material consumed and is at best only relatively accurate when carried to the proper dilution (6). Repeated dilutions, experience, and much care are required for any moderate degree of accuracy in measuring maximum hydrolysis of an enzyme solution. Using this method, Meyers and Reid (7) report that an accuracy of ±25 per cent was the best that could be obtained in determinations made on the diastatic activity of blood.

The estimation of amylolytic activity as adopted by McClure (2) is based upon the quantitation of the reducing sugar formed from starch hydrolysis by a modification of Folin-Wu's blood sugar determination (8). A buffered solution of duodenal drainage diluted 1:25 is allowed to hydrolyze a 2 per cent starch-phosphate mixture (pH 8.4) for one hour at 37°. The reducing sugar in an aliquot is then estimated. Inasmuch as glucose is used as the standard, the maltose resulting from the hydrolysis of the starch is expressed in mg. of glucose.

Leuders, Bergheim and Rehfuss (3) use Benedict's titration method (9) to estimate the maltose formed by starch hydrolysis. A 5 per cent starch solution made alkaline to phenolphthalein is used as a substrate to which undiluted duodenal drainage is added. N/10 sulphuric acid is added until the disappearance of color (pH 8). After incubation for one hour, the digestion mixture is titrated into Benedict's alkaline copper tartrate reagent. Amylolytic activity is expressed in terms of maltose.

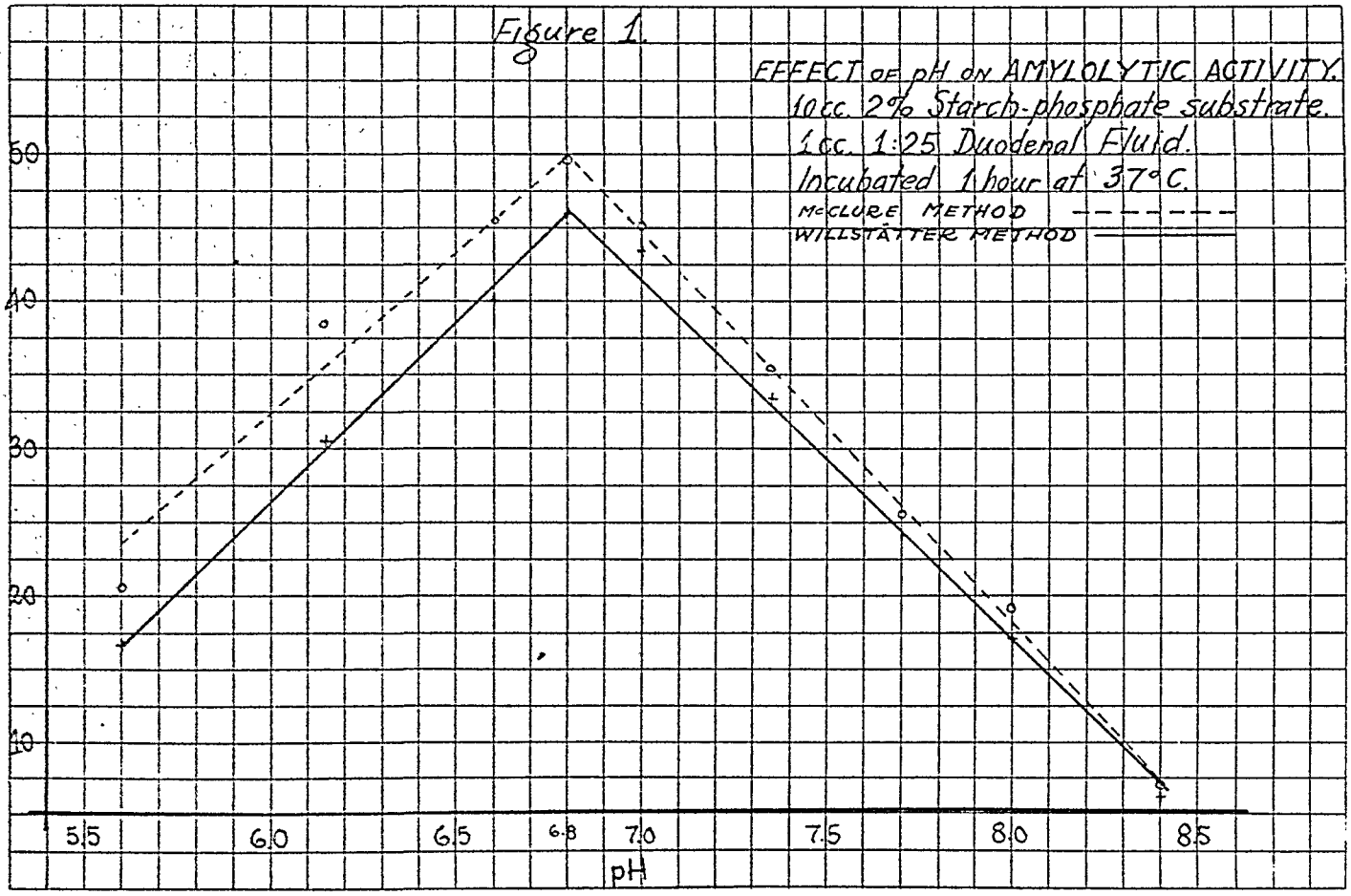
In the method of Willstätter, Waldschmidt-Leitz and Hesse (4), the measurement of enzyme activity is based upon a determination of the maltose formed when a buffered 1 per cent starch solution (pH 6.8) is acted upon by an enzyme solution for 15 minutes at 37°. The reducing sugar is then allowed to react with N/10 iodine in a solution made alkaline with an excess of N/10 NaOH and the remaining iodine titrated with thiosulphate. Results are expressed in mg. of maltose.

The method of Meyers-Bailey is one designed to measure the diastase in blood (5). In this method, the red color obtained by heating the hydrolyzed starch solution with picric acid and sodium carbonate is employed as the basis of a colorimetric determination. A glucose standard is used and results are expressed in terms of glucose.

EXPERIMENTAL

A comparison of the Wohlgemuth, McClure, Leuders, and Willstätter methods for measuring amylolytic activity was made. Typical results obtained by the four methods on the same enzyme sample are shown in Table 1. Determinations were run in triplicate and the values obtained by any one of the four methods check favorably; hence, they are satisfactory for comparative purposes when carefully performed. Because of variations in concentration of enzyme, concentration of substrate, time of incubation, and pH of the digestion mixtures, the different methods give widely varying results.

*From the Department of Physiology and Pharmacology, Northwestern University Medical School.
Submitted October 19, 1934.



Since it was desired to compare the relative merits of the methods under examination in regard to (1) accuracy, (2) minimum time required for the determination, and (3) simplicity, certain modifications had to be made in the procedures. In addition to placing the methods on a common basis for comparison, the changes instituted were made to alleviate certain defects such as optimum pH, dilution of enzyme, and certain minor factors that will be discussed.

TABLE I

Amylolytic Activity of Saliva. Using Four Different Methods. Typical Results.

Method Enzyme dilution Substrate	I. Wohlgemuth to endpoint 10 c.c. 1% starch	II. McClure 1 c.c. 1:25 9 c.c. 2% starch phosphate mixt.	III. Leuders 1 c.c. undiluted 10 c.c. 5% starch
pH	Approx. 7.0	8.4	8 to 9
	Wohlgemuth units	mg. glucose	mg. maltose
Test 1	110	5.6	336.5
2	123	5.4	339.8
3	117	5.0	323.5

Method Enzyme dilution Substrate	IV. Willstätter 1 c.c. 1:10 25 c.c. 1% starch
pH	6.8
	mg. Maltose
Test 1	26.7
2	28.3
3	27.1

Effect of pH and Concentration of Enzyme. Studies on the effect of pH on pancreatic diastase by Willstätter, Waldschmidt-Leitz and Hesse (4) have established optimum activity for this enzyme at a pH of 6.8. That an acid solution greatly inhibits human diastatic activity is a generally accepted fact; however, there seems to be some confusion regarding the effect of an alkaline medium on pancreatic diastase. McClure (2) used a substrate buffered to pH 8.4 for his work on amylolytic activity and Leuders and his associates were of the opinion that the employment of buffer mixtures offered no distinct advantages (3). Therefore, they carried out many of their determinations on an unbuffered starch solution. Willstätter and his co-workers (4) found that pancreatic diastatic activity was inhibited almost equally as the pH was shifted in either direction from an optimum of 6.8. This finding was confirmed by us in a number of series of determinations in which diluted duodenal fluid was allowed to hydrolyze a starch solution at different pH concentrations. Two per cent starch solutions, buffered over a range of from 5.6 to 8.4 with 0.2 molar phosphate-NaCl buffer, were incubated with 1 c.c. of duodenal fluid (diluted 1:25) and the amounts of reducing sugar formed determined by

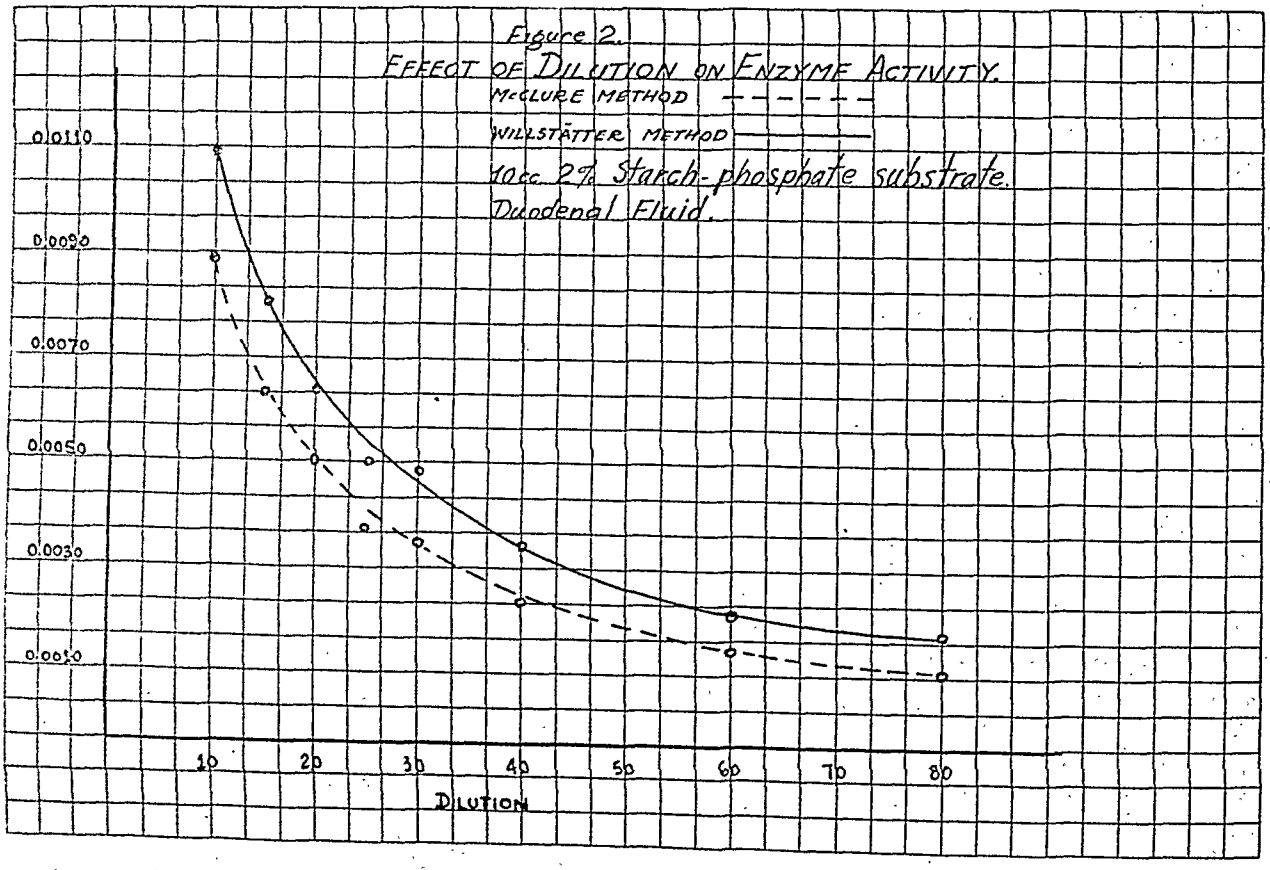
the Folin-Wu (McClure) and Willstätter methods. Typical results are shown in Table 2. In the determinations made after the method of Folin-Wu the reduced copper reagent was matched against a glucose standard (McClure) as well as against a maltose standard. Controls, containing 1 c.c. of boiled enzyme solution, were made on all determinations. In this regard it should be pointed out that in determinations made by the Willstätter procedure all of the control samples gave comparable values, whereas, by the copper reduction method (McClure) the control samples were greatly affected by pH concentration. Thus, the controls on values reported in Table 2 showed the following amounts of reducing sugar after the buffered starch solutions had been incubated for one hour at 37° and heated in boiling water for five minutes, the latter procedure being the method whereby enzyme activity is stopped in the McClure method:

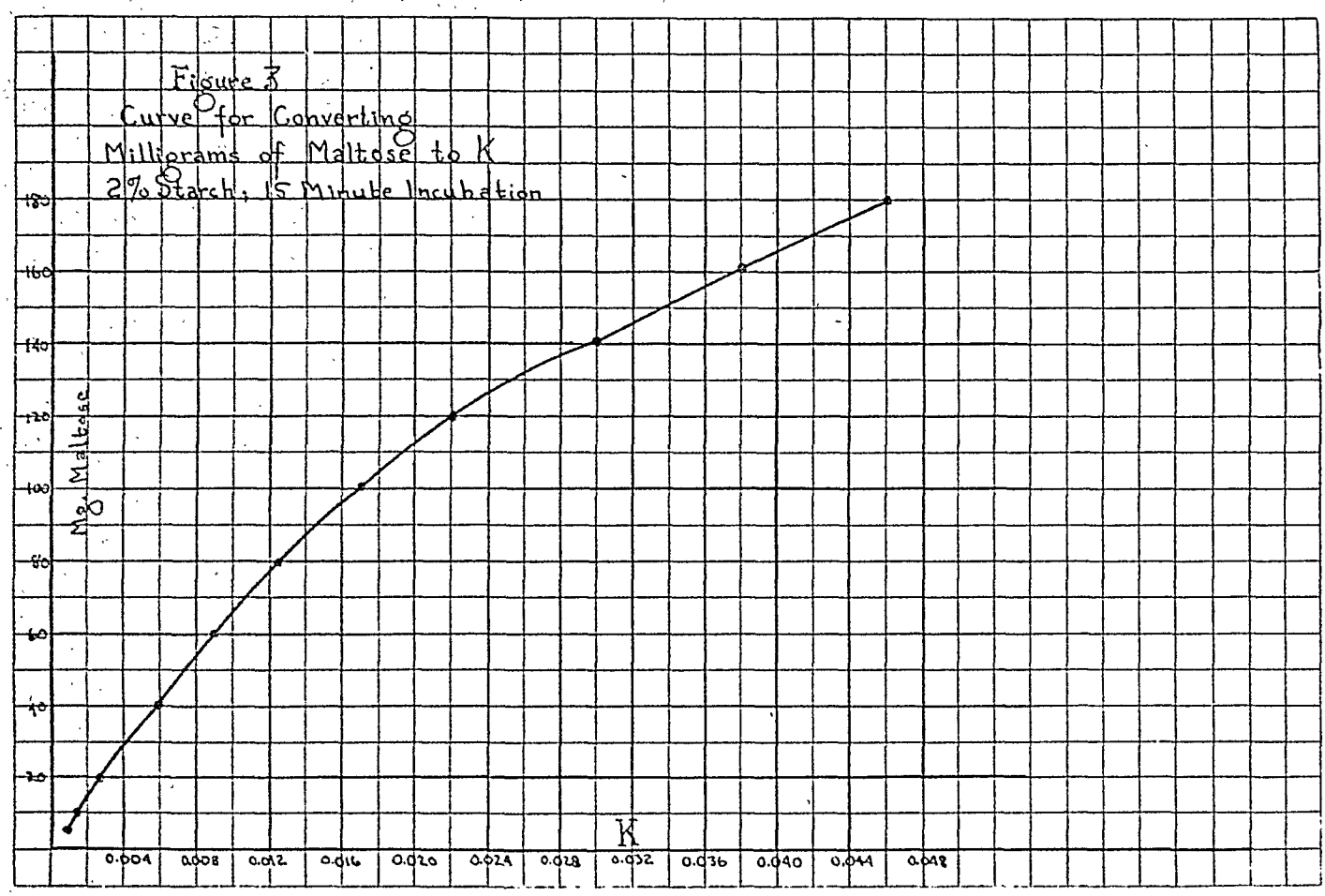
pH:	5.6	6.15	6.6	6.8	7.0	7.35	7.7	8.0	8.4
Mg. maltose in control:	0.0	1.8	2.9	3.7	4.8	7.1	10.3	13.9	18.1

Because of the increasing values of the control samples in the McClure procedure, when the net values obtained by the two methods are plotted as curves (Figure 1) the effect is such that at highly alkaline pH concentrations the curve of enzyme activity as measured by the McClure method approaches the Willstätter curve. From this observation it would appear that, in addition to inhibiting enzyme activity, the employment of an alkaline starch substrate results in one of two possible end results; either the presence of excess alkali favors a more rapid and complete reduction of the copper reagent, or the alkalinity of the substrate enters into and accelerates hydrolysis of the starch independent of the enzyme hydrolysis. As is shown graphically in Figure 1, amylolytic activity is affected greatly by the pH concentration of the substrate, the optimum occurring at a pH of 6.8.

Dilution of the Enzyme. While a few enzymes have been shown to react with an activity that is almost directly proportional to the concentration of the enzyme, in the case of many enzymes (lipase, sucrase, rennin, and trypsin) there is a difference in that a maximum intensity is soon reached and that subsequent concentration of enzyme is productive of no further increase in intensity.

Different dilutions of duodenal fluid, ranging from 1:10 to 1:80, were used with the view of determining a likely dilution that would assure maximum activity with a given strength of substrate. Typical results appear in Table 3. We have selected a dilution of 1:25 as a convenient dilution, although we feel that this point is one of little consequence so long as the dilution remains within the range of 1:10 to 1:40.





In Figure 2, the values obtained at different dilutions by both the McClure and Willstätter methods have been calculated and plotted to curve in terms of "K", the constant for the monomolecular equation which governs the hydrolysis of starch *(vida infra)*.

Standardization of Methods. A survey of the work on amylase studies by numerous investigators reveals a great variance of opinion as to the selection of a soluble starch suitable for enzyme analysis. Whereas the majority of German investigators have used Kahlbaum soluble starch, many workers in this country prefer a product of their own manufacture; others, particularly in connection with viscosimetric methods, employ Lintner's soluble starch. A number of analyses were made on Kahlbaum, Lintner (Merck), and Mallinckrodt starch, using the McClure and Willstätter methods to compare the values obtained when the same samples of enzyme solution (duodenal fluid) was allowed to act upon different starch substrates which were made up in 2 per cent solutions buffered to pH 6.8. Of the three brands examined the Kahlbaum starch appears to be the most soluble (Table 4); however, we are of the opinion that for comparative purposes any good grade of soluble starch satisfies the requirements. From the standpoint of convenience, the Kahlbaum starch remains in a homogeneous, transparent solution longer than the Mallinckrodt or Lintner products; the last brand is the most gelatinous of the three, a property which accounts for its preference in methods based on viscosity changes. For our comparative work on methods, both the Kahlbaum and Mallinckrodt products were used; routinely we find the Kahlbaum soluble starch very satisfactory.

For reasons discussed elsewhere *(vide infra)*, we are of the opinion that *maltose is the principle reducing sugar formed by the action of duodenal drainage fluid on soluble starch.* Because of this, it seemed desirable that the maltose be estimated as such and that the unit of diastatic activity be expressed as mg. of maltose. While, in any of the methods, the unit of activity is arbitrary, it seems irrational that a sample of maltose should be estimated against a glucose standard, especially since the two sugars have such distinctly different reduction values (10), (11), (12). Maltose reduces the copper reagent of the Folin-Wu and Benedict reagents and changes picric to picramic acid in the picric acid method much more slowly and incompletely than glucose. This fact does not interfere greatly with the Benedict or picric acid method except from the standpoint of time required to carry the reaction to completion. In the Folin-Wu method, however, the difference is marked. Table 2 shows the difference in values obtained by reading the reduced alkaline copper reagent against a glucose and a maltose standard.

TABLE II

Effect of pH Concentration on Amylolytic Activity. 10 c.c. 2% Starch-Phosphate Solution. Incubated 1 hour at 37°.

Method: Standard:	McClure Mg. Glucose:	McClure Mg. Maltose:	Willstätter Mg. Maltose:
pH.			
5.6	5.7	21.0	17.2
	5.8	21.2	17.4
6.15	10.2	37.9	31.2
	10.4	38.4	31.0
6.6	12.5	46.1	40.5
	12.3	45.8	40.2
6.8	13.4	49.5	46.7
	13.2	49.0	47.0
7.0	12.2	45.2	43.5
	12.5	45.4	43.2
7.35	9.5	35.3	32.8
	9.7	35.5	33.0
7.7	7.0	26.0	23.9
	7.5	26.6	24.3
8.0	5.2	19.3	17.5
	5.0	18.7	17.7
8.4	1.9	7.0	6.0
	1.8	6.7	6.3

For comparative purposes the following standards were used: For the Folin-Wu determination (McClure), weak and strong maltose standards containing 0.25 and 0.5 mg. maltose per c.c. were used. For a standard in the Benedict titration, the copper reagent used is made of such strength that 25 c.c. is equivalent to 50 mg. of glucose or 74.5 mg. of maltose (9). The factor for maltose was used in our determinations. Willstätter (4) has established a factor of 17.15 mg. of maltose for each c.c. of N/10 iodine used up in the hypoiodite reaction. In estimations of maltose made by the picric acid method of Meyers and Bailey, a solution of maltose (0.5 mg./c.c.) saturated with picric acid served as the standard.

TABLE III

Effect of Dilution on Enzyme Activity.

Substrate: Method: Incubation:	10 c.c. 2% starch-phosphate solutions. McClure: 1 hr. at 37°.	Willstätter: 15 min. at 37°.
Dilution:	Mg. maltose:	Mg. maltose:
1:10	107.1	46.2
1:15	88.8	35.8
1:20	76.8	29.7
1:25	65.0	24.0
1:30	58.1	23.0
1:40	45.1	17.2
1:60	28.0	10.9
1:80	21.8	9.1

In order to know that the modified methods were capable of detecting accurately the maltose formed by enzyme hydrolysis of starch, a series of determinations were made in which weighed amounts of chemically pure maltose were estimated. Ten c.c. portions of a 0.25 per cent maltose solution were buffered to pH 6.8, and the amount of reducing sugar was estimated according to the maltose-standardized methods of McClure, Leuders, Willstätter and Meyers-Bailey.

TABLE IV

Comparison of Starches: 10 c.c. 2% Starch-Phosphate Solutions (pH 6.8). 1 c.c. 1:25 Duodenal Fluid. Incubated for 1 Hour at 37°. Values Expressed as mg. Maltose. Determinations in Duplicate.

Starch:	Kahlbaum		Mallinckrodt		Lintner	
Method:	Willstätter:	McClure:	Willstätter:	McClure:	Willstätter:	McClure:
Test:						
1.	44.7	45.2	38.8	40.1	36.2	37.5
2.	41.3	42.2	38.9	39.6	36.4	37.0

TABLE V

Accuracy of Methods.

	McClure 25 mg. maltose	Leuders 25 mg. maltose	Willstätter 25 mg. maltose	Meyers-Bailey 25 mg. maltose
1.	25.25	25.40	25.20	25.75
2.	24.80	26.00	25.30	25.60
3.	25.70	25.70	25.25	25.80

Results are shown in Table 5. All four of the methods gave consistent results, and from a standpoint of comparative accuracy all four are satisfactory. It will be observed in Table 5 that the values obtained in the Willstätter method verify the hypothetical factor established by Willstätter and his associates.

The Presence of Maltase in Duodenal Drainage Fluid. Attention has been called to the fact that in the original McClure and Meyers-Bailey methods a glucose standard is used to estimate the reducing sugar resulting from enzyme hydrolysis of starch. Our reason for preferring a maltose standard is based on the fact that, unless an adequate supply of the enzyme maltase is present in duodenal drainage, maltose is the end-product of saccharogenic activity. Qualitatively both the disaccharide maltose and the monosaccharide glucose are reducing sugars; however, it is an accepted fact that their reducing properties are quite different. Because of this difference in reducing power, and because the hydrolysis of one molecule of maltose yields two molecules of glucose, a serious quantitative error would be introduced in the event that hydrolysis of some maltose to glucose took place without being taken into consideration. Such an error would be a constant one, and in such a case negligible, only if the amount of the enzyme maltase present remained constant. To determine whether maltose or glucose, or a mixture of the two sugars, should be used as standard, it was necessary to find out to what extent the enzyme maltase entered into the hydrolysis.

The question as to whether or not maltase exists in duodenal drainage in amounts sufficient to introduce a variable by subsequent conversion of

the formed maltose to glucose is one that has apparently had no consideration in the literature. Willstätter and Waldschmidt-Leitz (4) used a maltase-free glycerol extract in their work on enzyme activity of the pancreas. Maltase has been shown to have a very wide distribution in many tissues and animal secretions as well as their blood serum. According to Mendell and Mitchell (13), maltase has been found in the intestinal juice of man and animals by a number of investigators; but extracts of mucosa have been found to be far more active than the secretion itself. Recently (1933), Tauber and Kleiner (14) have shown that maltase is completely inactivated by trypsin in vitro.

TABLE VI

Tests for Maltase in Duodenal Drainage Fluid.

Patient	Enzyme	Mg. Maltose
Series i (approx. 75 mg. maltose)		
20-30	1 c.c. 1:25	80.3
	1 c.c. undiluted	80.2
20-8	1 c.c. 1:25	79.8
	1 c.c. undiluted	83.3
Control	1 c.c. boiled	80.6
Series ii (approx. 50 mg. maltose)		
20-4	1 c.c. 1:10	55.4
	1 c.c. undiluted	55.4
20-13	1 c.c. 1:10	48.5
	1 c.c. undiluted	54.5
Control	1 c.c. boiled	56.2

To ascertain the likelihood of a variable in our determinations due to the action of maltase in duodenal fluid, buffered samples of chemically pure maltose (pH 6.8) were incubated with various concentrations of freshly obtained duodenal drainage. These samples were treated by the same procedures used to determine starch-splitting activity. Under such conditions if maltase were a complicating factor in the results obtained in routine analysis some of the maltose should be hydrolyzed, evidence of which would be indicated by an increase in the reducing power of the digest due to the presence of glucose after one hour of incubation. The maltose solutions (pH 6.8) were made up to contain approximately 5 mg. sugar per c.c., a concentration comparable to that present in starch solutions after hydrolysis with duodenal fluid. Determinations were made on five different samples of human duodenal drainage fluid using both the Folin-Wu blood sugar method and the Willstätter determination. Controls containing an equivalent amount of boiled duodenal fluid served as a basis for comparison. Typical results appear in Table 6.

TABLE VII

Effect of $MgSO_4$ on Diastatic Activity. Activity in mg. Maltose.

Sample	Willstätter	McClure	Leuders	Meyers-Bailey
XI	130.2	143.7	141.2	173.3
1% $MgSO_4$	132.2	144.8	139.5	185.4
Control	131.8	143.7	142.0	151.3
	132.2	143.7	140.9	160.1
XII	95.4	139.0	139.0	146.1
5% $MgSO_4$	95.4	140.0	132.0	142.0
Control	95.3	143.0	136.5	142.5
	94.5	139.1	130.2	145.6

In no instance was there evidence of an increased amount of reducing sugar present over the amount present in the control determination. Evidently *active maltase is not present in human duodenal drainage fluid in quantities sufficient to become manifest under the conditions of the determinations.*

The Effect of $MgSO_4$ on Enzyme Activity. Since $MgSO_4$ is frequently used as an "excitant" in duodenal drainage observations, it was decided

TABLE VIII

Effect of Bile on Pancreatic Diastase. Values in mg. Maltase (Modified Willstätter Method)*

	Dog No. 1			Dog No. 2			Dog No. 3			Dog No. 4			Dog No. 5		
Series	Total	Control	Net	Total	Control	Net	Total	Control	Net	Total	Control	Net	Total	Control	Net
1.	98.2	18.9	79.3	140.8	18.5	122.3	116.4	17.8	98.6	79.0	17.1	61.9	88.0	18.3	69.7
2.	98.8	20.6	78.2	145.8	22.8	123.0	117.2	21.0	96.2	78.6	21.1	57.5	90.9	23.6	67.3
3.	97.6	18.0	79.6	131.6	21.6	110.0	116.3	18.7	97.6	76.2	19.7	56.5	88.3	20.5	67.8
4.	94.5	22.4	77.1	151.4	27.8	123.6	115.3	25.2	90.1	83.5	25.1	58.4	92.3	23.8	68.5
5.	123.0	45.5	72.5	165.0	40.8	124.2	116.7	29.4	87.3	95.0	37.6	57.4	109.5	45.3	64.2
6.				29.5	27.1	2.4	28.3	26.3	2.0	27.3	26.9	0.4	24.5	25.6	
7.	64.7	46.8	17.9	62.3	35.6	26.7	78.8	41.2	27.6	40.3	38.2	2.1	49.7	44.6	5.1
8.	47.7									39.3			44.6		
9.	119.8									93.5			109.0		
10.	102.0									78.7			87.5		

*Determinations by the method of McClure give comparable results.

Series	*Enzyme Solutions*
1.	1 c.c. Pancreatic Juice 1:25
2.	1 c.c. Pancreatic Juice 1:25 + 1 c.c. GB Bile 1:25
3.	1 c.c. Pancreatic Juice 1:25 + 1 c.c. Hep Bile 1:25
4.	1 c.c. Pancreatic Juice 1:25 + 1 c.c. Hep Bile 1:5
5.	1 c.c. Pancreatic Juice 1:25 + 1 c.c. GB Bile 1:5
6.	1 c.c. Hepatic Bile 1:5
7.	1 c.c. Gall Bladder Bile 1:5
8.	1 c.c. Boiled Panc. Juice 1:25 + 1 c.c. GB Bile 1:5
9.	1 c.c. Panc. Juice 1:25 + 1 c.c. Boiled GB Bile 1:5
10.	1 c.c. Panc. Juice 1:25 + 1 c.c. Boiled Hep. Bile 1:5

to ascertain whether $MgSO_4$ altered the enzyme activity of duodenal drainage fluid. A series of determinations were made in which $MgSO_4$ was *added to the enzyme solution* in concentrations of 1 and 5 per cent. The values obtained were compared with control determinations in which the same dilution of $MgSO_4$-free enzyme solution was employed. Two per cent starch solutions, buffered at pH 6.8, were used as substrate and the samples were incubated one hour at 37°. Results shown in Table 7 indicate that the presence of $MgSO_4$ in duodenal drainage fluid in concentrations up to 5 per cent does not alter the activity of pancreatic amylase.

The Presence of Amylase in Bile and the Effect of Bile on Amylolytic Activity. Löhner (15) and Fossel (16) have demonstrated the presence of amylase in the biliary secretion of mammals. Since bile is generally present to a variable extent in routine samples of duodenal drainage fluid, we desired to determine the effect of bile on pancreatic amylolytic activity. Samples of pure pancreatic juice, hepatic bile, and gall bladder bile were obtained by acute experiment from five dogs and determinations were carried out in which the effect of bile in varying quantities was observed during starch hydrolysis by pancreatic amylase. The detailed procedure with results appears in Table 8; the values reported represent the amount of maltose resulting from the hydrolysis of 15 c.c. of a 2 per cent starch-phosphate substrate (pH 6.8). Analysis of the determinations shown in Table 8 gives the following conclusions: (1) Hepatic bile, in 1:5 dilution, shows but little starch-splitting power, while gall bladder bile gives values on the average of ten times greater than hepatic bile (series 6 and 7). (2) The total amount of reducing substances present is slightly greater in the digests containing bile; however, because of increased values for the controls of such samples, the net values representing hydrolysis due to enzyme action are less (compare series 1 with series 2 and 5). (3) The enzyme activity displayed by bile (series 6 and 7) does not augment the activity of pancreatic juice quantitatively (compare series 1 to 7). This discrepancy is explained by the fact that the relationship between enzyme concentration and activity is a curvilinear one: the addition of small quantities of highly diluted biliary amylase to a highly active pancreatic juice does not result in a quantitative increase in the diastatic power of the combined pancreatic juice and bile. (4) The amount of reducing substances in the control samples containing bile increases directly as the concentration of the bile is increased. That the reducing substances present in samples in which bile has been mixed with pancreatic juice are not the result of a reaction of the latter with the former is shown by a comparison of series 5 and 9 and series 7 and 8; it will be observed that the *total* reducing substances (series 5) is unaltered when boiled bile is substituted for active bile (series 9), and that the control values obtained on boiled bile, in the absence of pancreatic juice (series 7), checks the values obtained when boiled pancreatic juice and active bile (series 8) are allowed to react with the starch phosphate substrate. (5) Inasmuch as duodenal drainage samples are routinely diluted 1:25 for analysis it appears that the presence of bile, even when the samples are made up of equal parts of concentrated gall bladder bile and pancreatic fluid, does not appreciably alter the results of determinations on diastatic activity (compare series 1 and 2). In the absence of pancreatic flow, the event of gall bladder evacuation would result in a sample of duodenal fluid composed largely of concentrated bile, which, when diluted 1:25, would show a decided deficiency in diastatic activity. Thus, despite the presence of small amounts of amylase in bile, the presence of bile does not interfere with the efficiency of routine determinations by the modified Willstätter procedure.

Comparison of Methods. Investigation of the methods standardized against maltose was carried out in which the reducing sugar formed by hydrolysis of starch was estimated by the four methods under examination. Dog's pancreatic juice and human duodenal drainage were used as sources of diastase. Twenty c.c. of a 2 per cent starch solution (pH 6.8) was incubated for one hour at 37° with 2 c.c. of the enzyme solution diluted 1:25, and the reducing sugars formed were estimated according to the methods of Folin-Wu (McClure) (8), Benedict (Leuders) (9), Willstätter (4) and Meyers-Bailey (5). In referring to these determinations as the "modified methods", it should be borne in mind that no modifications were made in the original methods for the estimation of reducing sugar except that maltose was substituted for glucose as a standard in the Folin-Wu and picric acid methods. The chief changes made in any of the procedures were those concerning substrate concentration, dilution of enzyme, and hydrogen ion concentration.

The results which are shown in Tables 9 and 10 represent typical values obtained by a large number of determinations in which the reducing sugars formed in a sample of hydrolyzed starch

TABLE IX

Comparison of Methods: Amylolytic Activity of Pancreatic Juice of Dog. 10 c.c. 2% Starch Solution (pH 6.8). 1 c.c. Pancreatic Juice (1:25). Activity Expressed in mg. Maltose. Determinations in Duplicate.

Willstätter	McClure	Leuders	Meyers-Bailey
Series i			
124.7	149.2	136.8	179.7
123.8	147.2	139.9	175.2
Series ii			
103.6	128.2	118.3	160.4
101.5	122.7	116.5	149.4

were estimated by the four methods under examination. All determinations were run in duplicate. Control determinations containing boiled enzyme solutions were made in each series of determinations. In all determinations on diastatic activity of both the dog's pancreatic secretion and human duodenal drainage the same relationship is seen to exist between the values obtained by the four methods. The picric acid determination gave the highest values, the copper reduction methods gave intermediate values, and the hypoiodite reaction gave the lowest values (see Tables 7, 9 and 10). (The explanation of this difference is given in the discussion.)

Pancreatic juice of the dog was obtained by acute experiment and its diastatic activity estimated by each of the four methods. Typical results with diastase expressed in mg. maltose appear in Table 9.

TABLE X

Comparison of Methods: Amylolytic Activity of Human Duodenal Drainage. 10 c.c. 2% Starch Solution (pH 6.8). 1 c.c. Duodenal Drainage (Diluted 1:25).

Sample	Willstätter	McClure	Leuders	Meyers-Bailey
I	110.5	136.8	121.8	168.7
	119.7	154.8	124.0	176.5
II	110.5	127.2	119.6	162.8
	108.9	120.0	121.8	161.3
III	123.7	138.7	136.5	156.2
	125.0	142.3	133.0	163.0
IV	88.8	97.3	93.2	115.6
	87.6	99.5	95.1	118.3

In our determinations on human duodenal drainage fluid diastase, samples were obtained by duodenal intubation, using intravenous injections of secretin to initiate response of the pancreas. Table 10 shows typical results obtained by the four methods under examination. Diastatic activity is expressed in terms of mg. of maltose.

DISCUSSION

Within comparatively recent years, many studies have been carried out on the enzymes of duodenal drainage, with the object in view of determining the state of pancreatic function in pathologic conditions in which enzyme activity was used to denote the functional state of the pancreas. A review of the literature reveals many conflicting conclusions and a lack of uniformity due, probably more than for any other reason, to the innumerable methods of investigation and the confusing arbitrary units and intangible values used to express enzyme activity. As we have stated, our investigation was made to determine which of the more commonly used methods was best adapted to routine analysis of duodenal drainage from the standpoint of accuracy, time and simplicity.

From the standpoint of comparative, but not quantitative accuracy, any one of the four methods examined is satisfactory. Referring to the values obtained by the different methods on the same sample of hydrolyzed starch (Tables 9 and 10), a definite relationship is seen to exist. The picric acid method of Meyers-Bailey has the highest values, the copper reduction methods have values that are intermediate, and the Willstätter method has the lowest values. In the case of results obtained by the copper reducing methods and the Willstätter method, our findings were in accord with those reported by Willstätter, Waldschmidt-Leitz, and Hesse (4). They attributed this difference to the selectivity of the hypoiodite reaction for maltose, whereas, in the case of the copper reduction methods the dextrins and secondary hydrolytic products as well as the reducing sugar enter into the reduction of copper.

Another contributing factor to higher results in the colorimetric procedures as well as in the Benedict titration is the employment of heat to hasten the action of the reducing sugar. The heating of partially hydrolyzed starch in an alkaline solution, which is the case in Folin-Wu, Benedict and picric acid procedures, would undoubtedly facilitate a breakdown of intermediate polysaccharides and a subsequent reduction of the reagent. Inasmuch as the control starch solution, to which boiled enzyme has been added, has undergone little if any hydrolysis such intermediate polysaccharides as are present in the hydrolyzed sample will not be present and the control would, therefore, fail to rule out this variable. The hypoiodite reaction is carried out at room temperature and the same factors apply to both the control determination and the unknowns. This theory seems to have been confirmed in our investigation, for although either method gives identical values on a known sample of maltose (Table 5), the copper reducing methods give appreciably higher values on a sample of starch. It seems likely that the same reasoning would account for the comparatively high values obtained by the picric acid method; however, if these factors remain constant they do not detract from the comparative accuracy of a series of determinations, since the reliability of any enzyme method depends upon constant relative results rather than specific quantitative reactions unaffected by intermediate reactions. The Willstätter determination has one outstanding advantage over the colorimetric method of Folin-Wu and the picric acid method in that the entire amount of reducing sugar formed is estimated by a single volumetric titration. The method as used in our routine analysis accurately determines amounts of maltose ranging from 0 to 150 mg. of sugar without alterations in the procedure. On the other hand, the colorimetric methods (Folin-Wu and Meyers-Bailey) are procedures designed for micro determinations on small quantities of sugar. Adaption to the determinations of large quanti-

ties of sugar such as is encountered in duodenal drainage analysis necessitates a dilution of 10 to 20 times of the digest in order that the concentration of reducing sugar in the unknown approximate that of the standards against which they are compared. Unless the unknown and standard agree quite closely when read in a colorimeter the error, which is multiplied by the dilution, becomes great. These rigid requirements almost require a foreknowledge of sugar concentration in order that the unknown be diluted to the desirable dilution. Frequently it becomes necessary to repeat a series of determinations because the unknown is not within the range of the standards. This criticism of the Folin-Wu and Meyers-Bailey methods is meant to apply to these methods only when used in determinations such as ours wherein 10 to 150 mg. of maltose is estimated.

Compared on the basis of time and simplicity, the Willstätter method has many advantages over the other three methods. A series of 6 or 8 determinations can be made in the time required for one determination by any of the other methods. In the case of the colorimetric methods, considerable time is spent in diluting and transferring aliquots from one tube to another, whereas, in an estimation according to the Willstätter method the entire determination is carried out in one flask. Although Benedict's method (Leuders) is without some of the disadvantages offered by the colorimetric methods, it is more indirect and more time-consuming than the Willstätter method in that obtaining the exact "end-point" is tedious.

From our investigation we have concluded that the Willstätter method is more suited to the estimation of diastase in duodenal drainage than the methods of Wohlgemuth, McClure, Leuders and Meyers-Bailey. It offers a convenient, time-saving, accurate determination that gives consistent results over a wide range of sugar concentration. The selectivity of hypoiodite for maltose is more specific than are the reducing agents of the other methods, and the units of activity are sufficiently high to be convenient.

The Willstätter Method Modified to Determine the Amylolytic Activity of Duodenal Drainage. Certain modifications of the method of Willstätter, Waldschmidt-Leitz and Hesse (4) were made to adapt the procedure to the estimation of diastase in human duodenal fluid. Determinations by the modified method are made as follows:

Pipette 15 c.c. of a 2 per cent soluble starch solution buffered to a pH of 6.8* into a 250 c.c. Erlenmeyer flask. Place in a constant temperature water bath regulated at 37° and, as soon as the starch solution has reached this temperature, add 1 c.c. of the enzyme solution (duodenal fluid) to be tested diluted 1 in 25 parts of distilled water. Keep at 37° for exactly 15 minutes. Remove the flask, add 2 c.c. N HCl to stop the enzyme action and then add 20 c.c. N/10 KI_2.** Add slowly with shaking 50 c.c. of N/8 NaOH. If the color has not faded after this addition add enough additional NaOH to obtain this color change.*** Let stand for 15 minutes, make distinctly acid with dilute H_2SO_4 (2 c.c. 10% H_2SO_4) and titrate the excess iodine with 0.05 N sodium thiosulphate.**** One c.c. of N/10 iodine is equivalent to 17.15 mg. of maltose. A control consisting of 15 c.c. of 2 per cent starch-phosphate containing 1 c.c. of boiled enzyme solution (diluted 1:25) is set up to determine the amount of iodine taken up by the starch. Ordinarily, a control determination on the stock solution of 2 per cent starch suffices for all determinations made using this lot of substrate. The method is based upon the following reactions:

(1) $2NaOH+I_2=NaI+NaOI+H_2O$.
(2) $NaOI+maltose=NaI+oxidation\ products$.
(3) $NaOI\ (excess)+NaI+H_2SO_4=Na_2SO_4+I_2+H_2O$.

The hydrolysis of starch to maltose is a reaction of the first order, for which the equation is $K=1/t \log \frac{a}{a-x}$. "t" is the time the enzyme was allowed to act; "x" is the amount of maltose equivalent to the iodine taken up (1 c.c. of N/10 iodine=0.01715 grams of maltose); and "a" is the maximum amount of maltose which can be set free by the starch, or 0.2250 grams. The value of "K" represents the number of units of amylase in the sample taken, and this multiplied by the dilution gives Willstätter units per c.c. For purposes of accuracy the value of K should be from 0.001 to 0.03; if less than the minimum the titration will be too low for accuracy, and if greater than 0.03, it indicates that the enzyme action has proceeded beyond the optimum range.

Amylolytic activity may be expressed either in mg. of maltose as derived from the thiosulphate titration or in terms of Willstätter units which involves solving the equation of the monomolecular reaction of K. Calculation:

[20 (c.c. iodine)]—[Excess iodine+iodine taken up by control] x 17.15=mg. of maltose.

$$K=1/15 \log \frac{0.2250}{(0.2250-\text{mg. of maltose determined})}$$

In Figure 3 appears a conversion curve for computing value of maltose expressed as mg. in terms of "K".

*The buffered starch solution is prepared by boiling 10 grams of soluble starch (Kahlbaum) in 250 c.c. of distilled water containing 2.92 gms. NaCl (0.2 M solution). To this is added 250 c.c. of phosphate buffer solution (70 c.c. 0.2M KH_2PO_4 and 180 c.c. 0.2M Na_2HPO_4). The final pH of the 2 per cent starch-phosphate mixture should be checked; however, in our experience this procedure gave a final pH of 6.8.

**12.685 grams pure resublimed iodine. 18 grams pure KI dissolved in 20 c.c. water. Add the iodine, dissolve with shaking, and make up to 1 liter. Standardize against N/10 or N/20 sodium thiosulphate.

***The color change in control samples will be from deep blue to a transparent blue; that in determinations will change from deep purple or brown to faint lavender or yellow as the case may be.

****As the end-point is approached, the blue color of free starch appears. If enzyme action has been sufficient to render the substrate devoid of free starch, 1 or 2 c.c. of starch solution is added and the titration continued until the end-point is reached, after which a few drops of 10 per cent H_2SO_4 should be added to the colorless solution to insure the technician that all of the free iodine has been liberated.

Under the conditions outlined under the modified Willstätter method, addition of starch solution as an indicator was not necessary in the case of any of our duodenal fluid samples; however, prolonged incubation time or the use of enzyme solutions more active than those used by us may make such an addition desirable. The accuracy of the method is most exact when the value "K" is between 0.001 and 0.03.

SUMMARY

Four methods for the determination of amylase in duodenal drainage and pancreatic juice

have been investigated from the standpoints of accuracy, time required and simplicity. Of the four methods, the Willstätter hypoiodite titration is best suited for clinical analysis of duodenal drainage fluid. It fulfills, to a greater extent than the methods of McClure, Leuders, and Meyers-Bailey, all of the requirements. This is true even after making modifications in the McClure and Leuders procedures that eliminate certain undesirable features.

1. The disadvantages of the original McClure method are: (1) A pH of 8.4 suppresses amylolytic activity. (2) The maltose formed by enzyme hydrolysis of starch is read against a glucose standard. (3) A series of determinations requires considerable more time than required to analyze the same number of determinations by the Willstätter method.

2. The disadvantage of Leuders' methods are: (1) Phenolphthalein interferes with the final titration of hydrolyzed starch into alkaline Benedict's reagent. (2) A 5 per cent starch solution does not remain homogeneous for any length of time. (3) In addition to one hour for incubation, each individual titration requires considerable time and patience if properly carried to an exact end-point.

3. The Willstätter method possesses no significant undesirable features; it is as accurate, if not more accurate, than the other methods, and it gives the nearest theoretical values when maltose is recovered quantitatively. The method, modified for determining amylase in human duodenal drainage fluid, is given in detail.

4. Amylolytic activity is affected markedly by the pH concentration of the substrate; optimum activity is obtained at a concentration of pH 6.8.

5. An enzyme dilution of one in twenty-five parts is within the range of optimum activity for the amylase in pancreatic juice and duodenal drainage fluid when used with a 2 per cent starch substrate buffered at pH 6.8. More concentrated enzyme solutions may be safely used.

6. Maltase is not present in duodenal drainage in amount sufficient to introduce a variable when the reducing sugar formed is estimated as maltose. This is true even when incubation of the substrate and enzyme solution is continued for one hour.

7. $MgSO_4$, present in duodenal drainage fluid in concentrations as high as 5 per cent, has no apparent effect on amylolytic activity as determined by the methods under examination.

8. The presence of bile in duodenal fluid does not interfere in determinations of amylolytic activity as measured by the modified Willstätter or McClure procedures.

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ABSTRACTS

BOWIE, D. J., AND VINEBERG, A. M.

Combined Histological and Physiological Study of Gastric Secretion under Prolonged Vagal and Histamine Stimulation. Trans. Roy. Soc. of Canada, Vol. 28:126, 1934.

Variations in stimulation of the gastric glands seemed to activate different cytological elements in the gastric mucosa. Strong vagal stimulation gave a secretion high in peptic activity and acid content. Histamine stimulation produced a secretion extremely low in pepsin but high in acid content. On histological examination it was found that after strong vagal stimulation the zymogenic granules in the peptic cells were greatly reduced in number, whereas after histamine stimulation such reduction was not observed. In both types of the experiment the corresponding stimulation lasted for several hours and produced approximately equal volumes of gastric juice (from 800 c.c. to 1000 c.c.). Thus the histological evidence confirms the physiological conception of independent regulation of the activity of certain cytological elements of the gastric mucosa.

B. P. Babkin, Montreal, Canada.

FAUST, ERNEST CARROLL, AND KAGY, EDWIN S.

Studies on the effect of feeding Ventriculin, Liver Extract, and raw liver to dogs, experimentally infected with Endamoeba Histolytica. Amer. Jour. Trop. Med., 14:235-257, 1934.

A sacrifice of 19 dogs experimentally infected with *Endamoeba Histolytica*, to learn the effect of feeding Ventriculin, Liver Extract, and raw liver in the course of the infection. A problem perhaps of academic interest but of no practical value in the treatment of human amebic infections, since dietary measures assume only secondary importance as compared to the chemotherapy of this infection.

W. C. Boeck.

SECTION III—*Nutrition*

The Complete Treatment of Pernicious Anemia*

By

RUSSELL L. HADEN, M.D.
CLEVELAND, OHIO

SINCE the advent of liver therapy in pernicious anemia, many articles have been written on the treatment of this disease. The number of liver substitutes alone and in combination offered for clinical use is legion. Preparations for oral, intramuscular and intravenous use now are available. Recommendations concerning the use of these agents include single massive doses orally at infrequent intervals, a single intravenous injection periodically, intramuscular injections at varying intervals, and different combinations of oral, intravenous and intramuscular treatment. It is apparent, however, from recent articles and from observation of patients incompletely treated that still there is much confusion and lack of knowledge concerning the management of this serious and commonly observed disease. Minot[1,2] well has stressed the need for treating pernicious anemia from a quantitative standpoint and for supplying enough potent material throughout life for the individual patient afflicted with this disease.

Clinically, there are three phases of pernicious anemia, the gastro-intestinal, the hematologic and the neurologic. The older idea that the disease is caused by the action of a toxin, derived from the gastro-intestinal tract, acting on the blood cells, bone marrow and spinal cord has been abandoned.

All observers, as a result of the brilliant work of Castle and his coworkers, now agree that the disease belongs in the deficiency group and is due to the lack of a substance formed by the interaction of an intrinsic factor secreted by the stomach and an extrinsic factor supplied by the food. The constant achlorhydria is the simplest clinical indicator of the gastric defect. Besides the gastric defect, glossitis and atrophy of the tongue are very commonly observed, and diarrhoea frequently occurs. While the gastro-intestinal phase concerns largely the primary defect in gastric secretion, the glossitis and diarrhoea usually are secondary to the deficiency.

The anemia and characteristic blood findings result from a lack of the specific substance normally formed by the interaction of intrinsic and extrinsic factors. This substance is necessary for the normal growth of new red cells in the marrow at the megaloblast stage. In the absence of this substance erythrocytes develop to a certain stage and die *in situ* since they are unable to grow to the point at which they normally would emerge from the marrow. Many of the cells which do get out are larger than normal, hence the characteristic macrocytosis. The lemon yellow color of the skin or clinical jaundice is due to an excessive destruction in the marrow of erythrocytes which are unable to mature, with consequent increase in bile pigments in the plasma. The red color of the marrow of the long bones in the active stage of pernicious anemia is due to the great accumulation of cells which cannot mature because of the lack of the specific substance. The leucopenia and thrombopenia result from the mechanical blocking of the leucocytes, thrombocytes and megakarocytes in the hyperplastic marrow. All the characteristic blood findings in pernicious anemia, such as macrocytosis of the erythrocytes, excessive maturity and decreased number of leucocytes, lowered platelet count, and increase in bile pigments of the plasma are due to the interference with growth of red cells in the marrow, resulting from the lack of the specific substance necessary for the normal development of erythrocytes.

The neurologic phase of pernicious anemia includes the characteristic involvement of the posterior and lateral columns of the spinal cord, the frequent peripheral neuritis, and the infrequent cerebral disturbances. These symptoms formerly were ascribed to the anemia and some unknown toxic agent. Now they are interpreted as due to the loss of something necessary for the integrity of nerve tissue. It is still not clear whether this is the same substance necessary for normal erythrocyte formation.

Usually the neurologic phase of the disease accompanies the hematologic phase. It may occur with only slight changes in the blood so that the neurologic changes overshadow the blood findings. Rarely, if ever, does the neurologic phase develop in an untreated patient in the entire absence of macrocytosis, so it seems the red cells always must

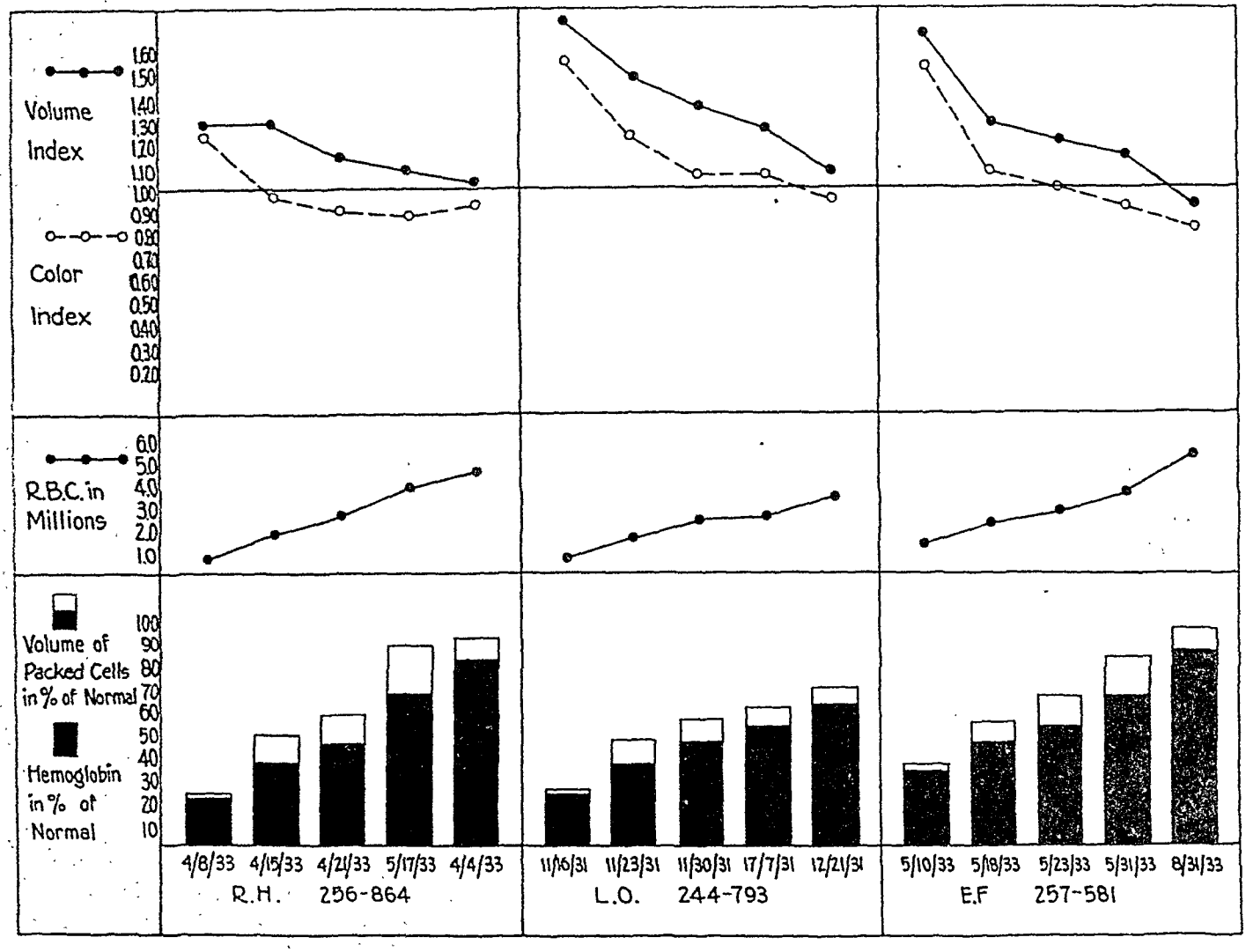
*From the Division of Medicine, The Cleveland Clinic.
Submitted October 12, 1934.

show evidence of a deficiency if the integrity of nerve tissue is impaired. This is strong evidence that the substance concerned in the two phases is identical. The marked improvement in neurologic lesions which is frequently observed following treatment with the substance specific for normal red cell formation also speaks strongly for the identity of the two substances. It seems certain that the deficient substance is not a known vitamin or other preformed body, since treatment with these alone helps little. For the formation of this protective substance the interaction of an intrinsic and extrinsic factor seems required, just as for the hematopoietic protective substance. Strauss and Castle[3] suggest that the substrate or extrinsic factor may be vitamin B_2 for the substance required for normal erythocyte formation, and vitamin B_1 for the substance necessary for the normal integrity of nerve tissue and the intrinsic factor may be the same in both instances.

It is apparent, then, that all the symptoms of pernicious anemia except those incident to the achlorhydria, namely glossitis and atrophy of the tongue, anemia, macrocytosis of erythrocytes, increased icterus index, thrombopenia and leucopenia, neuritis and subacute combined degeneration of the spinal cord are secondary to and result from a deficiency in the protective substance or substances normally present. So far as is known, once the deficiency is established, it is permanent. The treatment of all phases of the disease is thus entirely dependent on adequately and continuously supplying the missing factor or factors.

Deficiencies in other than the specific substance also occur commonly in pernicious anemia, probably because the absorption and utilization of food factors are interfered with in patients having achlorhydria and the gastric defect. The general

Fig. 1. The course of the blood in properly and completely treated pernicious anemia. There is a rapid rise in the hematocrit reading (volume of packed cells). The hemoglobin rises also but the increase in hemoglobin often is less than the increase in cell mass so a hypochromia develops. If this persists, iron should be given although there is usually a sufficient reserve store of iron to supply any iron need. The red cell count rises and the volume and color indices fall. Often the color index is normal long before the volume index has reached the normal line. The blood is never normal until the volume index has reached 1.00 and remained so.



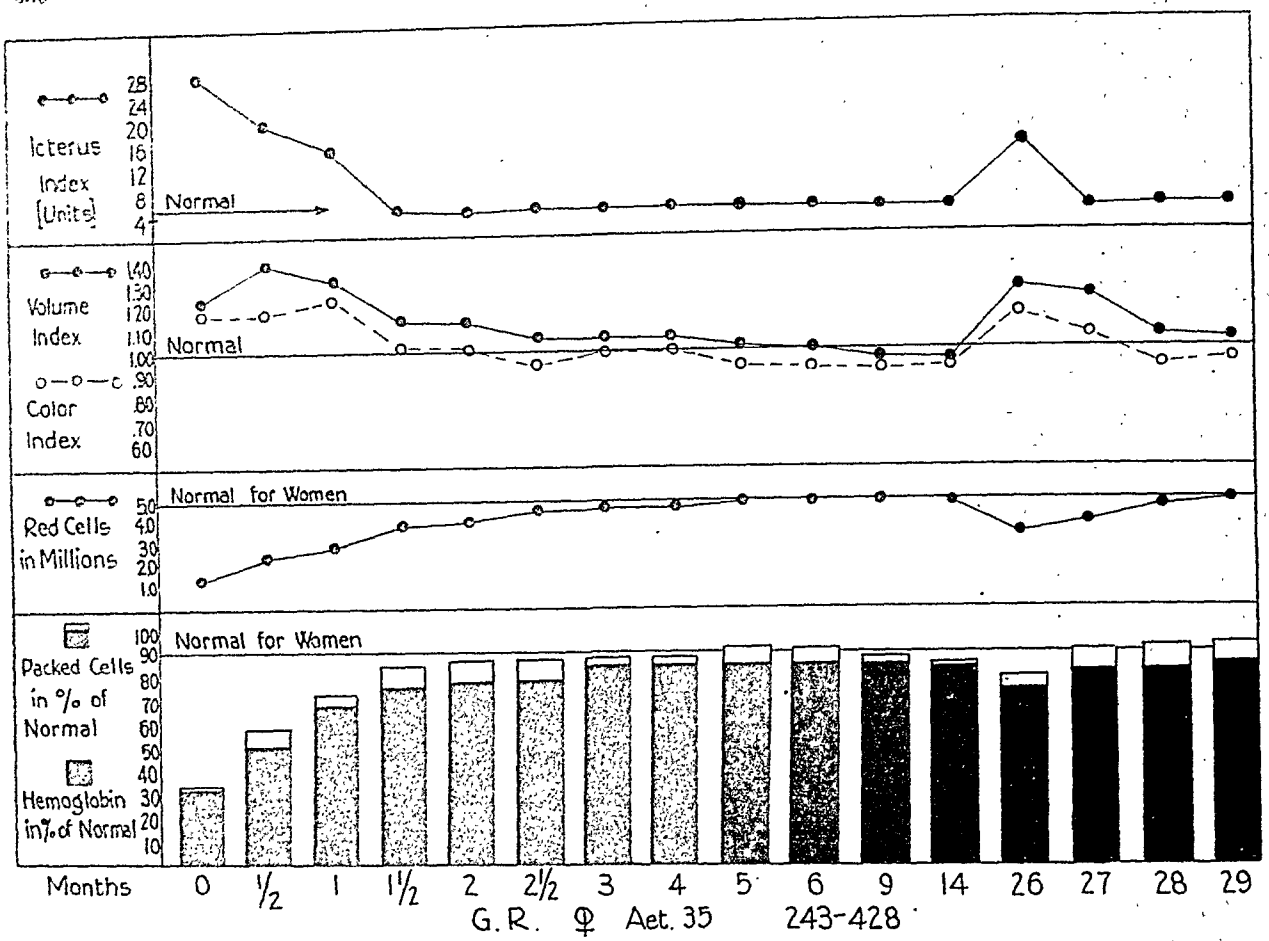


Fig. 2. Blood findings over two and one-half years in young woman with a history of anemia for three years and marked combined system disease. She was entirely disabled with predominant lateral column involvement. A correct diagnosis had been made but treatment had been very irregular. For economic reasons treatment has consisted entirely of liver by mouth. Note that the blood rapidly returned to normal and remained so until the patient stopped eating liver for a time. No significant anemia developed but the icterus index rose indicating excessive death of immature erythrocytes in the marrow, and the volume index promptly became abnormally high. With resumption of liver treatment the blood again returned to normal. A cord lesion is very apt to develop or progress during such a period of deficiency, although the anemia may be of no significance.

nutrition is impaired as shown by the rapid gain in weight observed in patients properly treated, and the finding at times of other known vitamin deficiencies with pernicious anemia, such as beriberi, pellagra, sprue and of an idiopathic iron deficiency. These deficiencies usually are automatically corrected by the diet, the general measures and the specific therapy applied in cases of pernicious anemia. Often the other missing protective substances need to be supplied continuously in larger amounts since intestinal absorption is always interfered with by reason of the achlorhydria. The successful treatment of pernicious anemia depends on satisfying adequately the deficiency responsible for the disease. The problem is to supply completely the missing substance, not to give liver or some liver substitute in certain amounts so many times a day, since the deficiency is quantitative and varies greatly in different patients. *The disease once established must be treated continuously and without interruption during the remainder of the patient's life.*

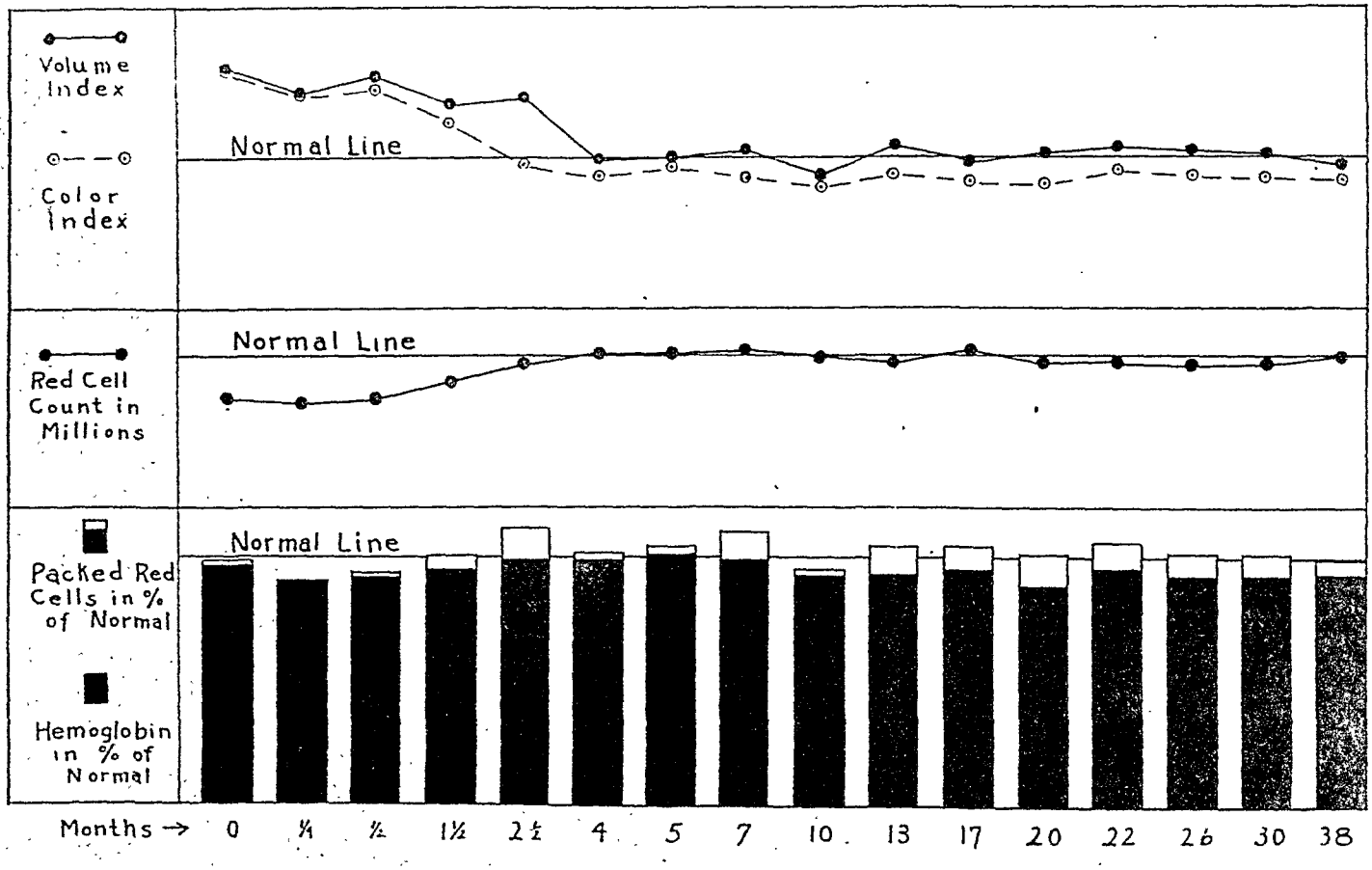
What are the criteria for determining the deficiency and measuring the efficacy of treatment? Clinical criteria of the deficiency are the anemia, glossitis and parasthesias. The progression or development of such symptoms during treatment is proof of activity of the disease, and the continuation of a deficiency. Often the anemia is not sufficiently marked to be detected clinically, and the neurologic phase may persist as the result of permanent irreparable damage to nerve tissue, even with complete treatment. A more sensitive indicator is required. The one characteristic blood finding in pernicious anemia from the laboratory standpoint is macrocytosis of the erythrocyte. This is the first hematologic manifestation of the disease and persists when all other signs are gone.

so is by far the most valuable indicator of the deficiency. Even when the neurologic signs overshadow all others, macrocytosis is almost invariably present if the disease is untreated. If glossitis and atrophy of the tongue are due to active pernicious anemia, macrocytosis also is found. This one criterion is a constant, accurate, and dependable measure of the deficiency and also the efficacy of treatment. The blood is never normal if macrocytosis persists. The presence of a macrocytosis is absolute evidence of an incompletely supplied deficiency.

Macrocytosis of the erythrocytes is determined from the red cell count and hematocrit readings. The volume of the mean cell may be calculated in cubic microns. The actual measurements, however, are not so significant as the size of the cell relative to normal. The volume index which shows the volume of the mean cell relative to normal is the best measure of the cell volume. The technic for determining the volume index and cell volume has been described elsewhere[4]. Macrocytosis is seldom observed excepting in pernicious anemia. Macrocytosis with achlorhydria is almost absolute evidence of pernicious anemia. In determining the volume index, normal figures should fall between 0.95 and 1.05. Borderline figures are 0.90 to 0.95 and 1.05 to 1.10. A volume index below 0.90 or above 1.10 is definitely abnormal. An adequately treated patient with pernicious anemia will always show a return of the volume index to 1.00 or lower, and continue at a normal level unless a deficiency again develops. The amount necessary for such a result must be determined for each patient.

The neurologic lesion is by far the most serious clinical phase of pernicious anemia. The characteristic degenerative lesion involves predominantly the posterior and lateral columns of the spinal cord. It has been thought in the past that once the lesion has developed, repair is impossible. With liver therapy excellent symptomatic improvement in the neurologic lesions has been reported. Other observers report progression of the neurologic signs and symptoms in patients undergoing specific therapy or the development of such

Fig. 3. Successive blood examination in a patient with combined system disease. The neurologic involvement was predominant in the posterior columns, with a resulting ataxia which confined the patient to a wheel chair. Note that the hematocrit reading and hemoglobin were practically normal when the patient was first seen. The macrocytosis was well marked, however, as shown by the high volume index. With no significant change in the hematocrit reading or hemoglobin the volume index has returned to normal and remained so. The patient has taken liver extract every day and eaten some liver regularly. He has made a complete symptomatic recovery and returned to his work as a farmer, although the signs of posterior column involvement have not completely cleared up.



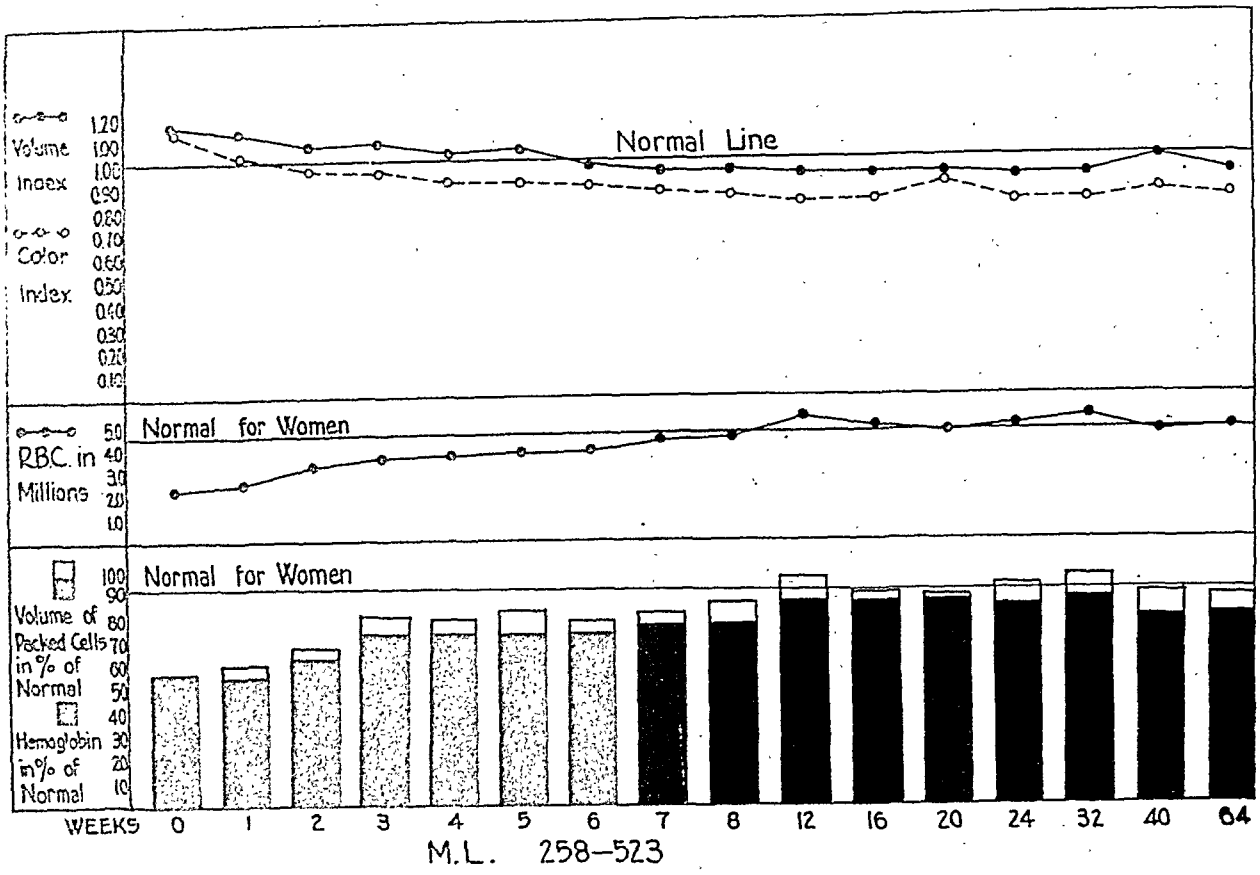


Fig. 4. Findings in patient with extreme combined system disease, including a cord bladder with inability to void. The diagnosis had been correctly made and the patient had had incomplete treatment for three years. When admitted she was completely disabled from the cord lesion and confined to a wheel chair. She has had intensive dietary, oral and intramuscular therapy and has made almost a complete symptomatic recovery. She has no bladder symptoms, walks without any assistance and has returned to work. Note that the volume and color indices have been kept well below the normal line by the intensive treatment. The patient's deficiency has been completely and continuously supplied with a most excellent clinical result.

lesions when none had been present before the institution of therapy. Such a course is due to insufficient and incomplete therapy. It is apparent to all that more intensive and longer continued specific treatment is required to influence the neurologic lesion than is necessary for relief of the anemia. Excellent results can be achieved with proper therapy, however.

Symptoms due to the gastro-intestinal phase of the disease, such as glossitis and diarrhoea, usually respond quickly to specific therapy. The achlorhydria remains permanently.

Since pernicious anemia often is complicated by other deficiencies, it is most important to give a complete diet with added vitamin B. The liver extract supplies vitamin B_2 but B_1 must be supplied in the food alone or by the addition of wheat germ and yeast products. I see little use in prescribing dilute hydrochloric acid unless symptoms such as gaseous indigestion or gastrogenic diarrhoea be present for which acid would be given if the patient had an achlorhydria apart from pernicious anemia. As a rule, iron is not necessary. Sometimes there is a deficency in iron absorption such as is seen in idiopathic hypochromic anemia requiring the addition of iron. An iron deficiency may develop with rapid cell regeneration in response to treatment, especially if the volume and color index are not very high before beginning treatment. In such cases iron may be needed after the reserve store is depleted.

What is the best method of administration of specific therapy? I have adopted the plan of giving an intramuscular injection of a parenteral liver extract derived from 100 grams of liver daily for two weeks. After this period a similar injection is administered weekly for three months and then every two or four weeks as the individual patient requires. If the blood count is low at the beginning of treatment, the appetite is usually poor, so the patient is allowed to eat as he desires. Within a week after the beginning of treatment the patient is started on a special diet for anemia[5] and is encouraged to eat liver every day. In the

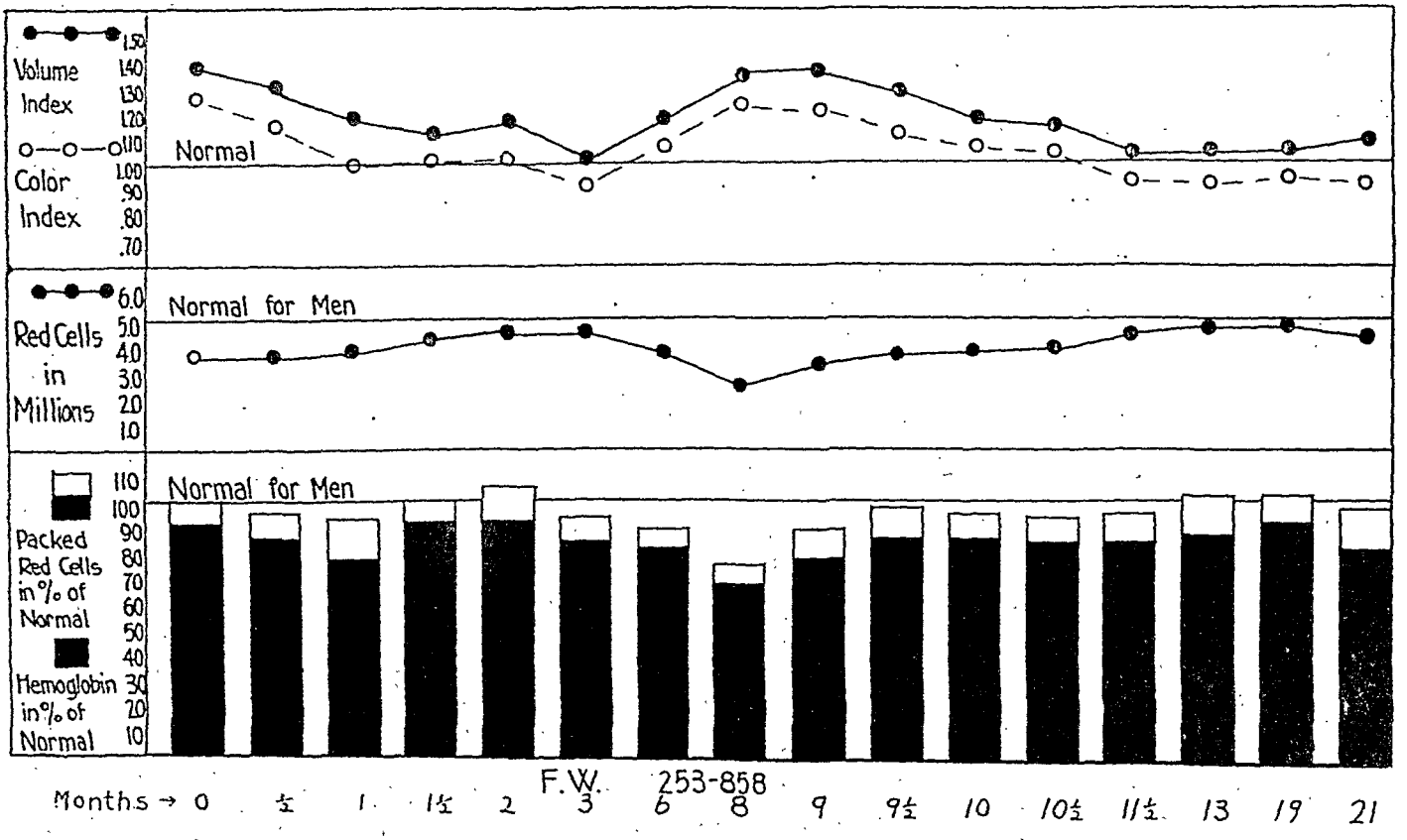
less serious cases after improvement is well under way, the oral administration of liver or any potent liver substitute in adequate amounts may be substituted for the intramuscular injections. The diet should be continued permanently. The amount of liver substance to be taken by mouth is determined on the basis of the blood and clinical findings. In any event, it is most valuable to give an intramuscular injection of liver extract once a month for an indefinite period of time in addition to the special diet and the oral therapy.

If the patient has a predominant or well-defined neurologic lesion at the beginning of therapy, or shows signs of developing such a lesion, more intensive therapy is instituted. After the preliminary fourteen-day period of daily injections, the eating of liver daily as part of the special anemia diet is insisted upon. After the first week of treatment a liver substitute is given by mouth also in adequate amounts each day. Vitamin B is also added to the diet as wheat germ, yeast or yeast extract. Intramuscular injections are continued indefinitely at least twice a week. This plan of treatment is not fixed, however, but is varied in the light of the patient's needs as determined by the volume index and the clinical course.

A complete blood study is done every week for the first two months, then monthly for the following four months and at three-month intervals thereafter, if possible. No patient with pernicious anemia should go longer than three months without a careful blood examination as a deficiency in treatment can be detected by careful studies of the blood long before symptoms or physical signs indicate an inadequacy. During the first weeks of treatment, reticulocyte counts are made daily.

By following this plan of intensive dietary, intramuscular and oral therapy, controlled by frequent complete blood studies, I have not seen a single patient whose blood could not be returned to normal and kept so, nor a single patient in whom neurologic lesions developed during the course of intensive treatment. Every patient with neurologic involvement at the beginning of treatment has shown some improvement; in many instances the improvement has been most striking. The good results have been attained only by supplying abundantly the lacking specific substance so as to keep the volume of the mean cell normal as indicated by the volume index. In cases where the neurologic involvement is marked, the volume index has been kept constantly well below normal

Fig. 5. The blood findings in an incompletely treated patient. Note that the volume index has only once been found normal, indicating that the patient has continued to have a deficiency. This patient is a young man, aged 26, with a history of anemia for two years before admission and frequent attacks of diarrhoea. The poor result in this case has been due to the poor co-operation of the patient. After the volume index had reached normal, treatment was not followed properly.



by more intensive therapy. Such a plan of treatment requires the co-operation of the patient. This can usually be assured by explaining to the patient the nature of the disease and the purpose of the treatment and by frequent blood examinations.

The blood findings in patients in relation to therapy are shown in the accompanying illustrations.

SUMMARY AND CONCLUSIONS

Pernicious anemia in all its phases is a deficiency disease.

The treatment of the disease consists in adequately supplying the deficiency.

The best indicator of the deficiency is macrocytosis of the erythrocytes.

The efficiency and adequacy of treatment can be measured by measuring the volume of the red cell.

The deficiency responsible for the disease is never supplied so long as macrocytosis of the erythrocytes persists.

Supplying too little of the missing substance or substances allows the disease to progress and neurologic complications to develop.

Supplying an excess of the missing substance can do no harm as the excess is probably stored for future use when more is needed as in infection or when utilization is impaired with advancing age or the development of arteriosclerosis.

With proper treatment the blood should be kept normal and neurologic involvement prevented.

The neurologic symptoms should improve with intensive therapy.

A method of therapy which has proved most satisfactory in our hands is outlined.

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ABSTRACTS

BURNETT, FRANCIS LOWELL, AND OBER, FRANK ROBERTS.

Arthritis, Anabolic Nutrition and Health. A Study of the Nourishment and Health of Joints. Am. Jour. Med. Sc., p. 93, July, 1934.

This work is based upon the study of 152 patients affected with arthritis. According to the authors etiologic factor is the failure of nutrient material to construct or preserve normal bone and cartilage. To correct this metabolic disorder the authors formulated a system of dietetic and hygiene control designed to prevent undue colonic motility. Gradual improvement resulted when the feces became segmented—the so-called "unit feces" of Burnett. About 25 per cent of the patients were restored to health and 50 per cent were improved. Twenty-five per cent remained the same or became worse. This record would seem to be a remarkably good one for the treatment of arthritis.

The intestinal rate is an index of absorption. Experimentally, the evening meal is marked by means of millet seeds or charcoal. The average rate in healthy adults is 62 hours for the first appearance of the marked meal and 134 hours for its disappearance from the feces. When a patient has reached this intestinal rate he is in a state of "anabolic nutrition". Food absorption is complete and no digestible, nutritive material leaves the body.

The question of the normal rate of intestinal motility is interesting. The majority of clinical gastro-enterologists would consider the authors' figures to indicate a rather severe form of constipation. Hurst and other X-ray observers place the rate of colonic motility at much lower figures. Hurst defines constipation "as a condition in which none of the residue of a meal, taken eight hours after defecation is excreted within forty hours".

The work reported by Burnett and Ober should stimulate further study of this important subject. If these authors' deductions are admissible, the vast majority of the human race would seem to be affected with some degree of malnutrition, a "conditioning" which may be followed by numerous forms of disease-syndrome, one of which may exhibit itself as "arthritis".

Horace W. Soper, St. Louis, Missouri.

G. MARAÑON, P. SALA AND G. ARGUELLES.

Endocrinology. Digestive Symptoms in Chronic Suprarenal Insufficiency (Addison's Disease). 18: 497-504, July-August, 1934.

A study of 160 cases of unquestionable Addison's disease observed by these workers, the following is the incidence of digestive symptoms:

	Cases	Per Cent
Intense hunger*	3	1.8
Anorexia	142	88.7
Dyspepsia	61	38.0
Nausea and sickness	39	24.3
Gastric ulcer	3	1.8
Diarrhoea	45	28.0
Constipation	35	21.8
Pseudoperitonitis	11	6.8
Hiccough	43	26.8
No symptoms	19	11.9

*In those subjects with intense hunger, this symptom apparently was not related to hypoglycemia or associated ulcer.

Many of the digestive symptoms were ascribed to hypochlorhydria or achlorhydria which were present in one-half of the cases in which the gastric juice was studied.

Dwight L. Wilbur, Rochester, Minnesota.

SECTION V—*Therapeutics*

Treatment of Functional Vomiting*

By

C. H. DRENCKHAHN, M.D.

and

D. L. WILBUR, M.D.

ROCHESTER, MINNESOTA

SINCE vomiting is a symptom of disease, it is essential in treatment to recognize the underlying disease even though it is obscure. Vomiting is produced as a result of organic disease, involving the gastro-intestinal tract or unrelated organs, of functional disease or of neurosis. The clinical picture presented by patients with functional vomiting and a method of treatment which we have found very successful will be considered here. In order that there may be a clearer understanding of the factors concerned in the mechanism of vomiting and the *rationale* of the treatment to be described, a brief review will be given of the most acceptable theory of vomiting.

In higher animals, including man, the act of vomiting is regulated by a vomiting center. The act itself consists of closure of the pylorus, contractions of the pyloric half of the stomach, relaxation of the cardiac half, and of the esophagus, closure of the glottis with inhibition of respiration, and finally contraction of the muscles of the abdominal wall and muscles of respiration. The act is complicated and must have a co-ordinating center. This center seems to be situated in the sensory nucleus of the vagus nerve in the floor of the fourth ventricle of the brain. The vomiting center is continually receiving stimuli from various parts of the body, especially the abdominal viscera. Ordinarily the majority of the stimuli are subminimal and do not arouse a response. The threshold for response to stimuli in the vomiting center can be so lowered that ordinarily subminimal stimuli can arouse a response, as for example, in vomiting caused by apomorphine. It seems reasonable to suppose that the threshold for response to stimuli in the vomiting center is lowered in subjects with functional vomiting. In fact, individuals afflicted with functional disorders seem to have a lowered threshold for the reception of some or all stimuli. Consequently such persons may become conscious of normal physiologic processes such as the heart-beat, the pulsation of peripheral vessels, or the movements of the colon, whereas, in normal persons these stimuli are subminimal and never register in the higher centers.

The clinical features of functional vomiting are characteristic. The condition most often afflicts young, unmarried women who present other psychoneurotic tendencies. In such cases, Alvarez has pointed out the frequency of a family history of nervous disorders. The vomiting may be incited by fear, excitement, mental strain or shock, overwork, or mental depression. It is likely to recur periodically. There is rarely any loss of appetite. The patient usually vomits easily, without premonitory symptoms such as nausea, trembling, cold perspiration or fainting. Usually vomiting occurs within half an hour after eating, rarely after two hours have elapsed; the patient is always able to reach a receptacle. As a rule, there is no relationship between vomiting and the quantity or quality of food eaten. Vomiting may occur frequently over a long period of time without any great effect on the general health of the patient. In fact, usually not so much weight is lost as would be anticipated in individuals who, as a result of organic disease, vomit frequently over a long period. The stomach is not completely emptied, nor is the vomitus copious or retentive in type. Often a lowered basal metabolic rate is present. This conforms to the general inactivity of the individual.

REPORT OF CASES

Case 1—An unmarried woman, aged nineteen years, registered at this Clinic, June 11, 1934, because of persistent vomiting of three and a half years' duration. At ten years of age the patient had been operated on, elsewhere, for a ruptured appendix, after which drainage had persisted for thirteen weeks. The only immediate residual symptom was constipation. At fifteen years of age, the patient finished grade school and remained at home with her mother, who ran a farm in Montana. Life was apparently not very happy for the patient because she was with her mother only and was unable to associate with others of her age. Shortly after she stopped going

*From the Division of Medicine, by agreement with the Authors and the Editorial Department of the Mayo Clinic. Proceedings of the Staff Meetings, Mayo Clinic, August, 1934.

to school, vomiting began to occur at irregular intervals. Details could not be recalled, but the vomiting was apparently similar to that present at the time of admission to this Clinic. A few weeks after onset of the vomiting an operation for abdominal adhesions was performed elsewhere, but one week after this operation vomiting recurred. From the age of fifteen and a half until seventeen years, vomiting occurred after approximately half of her meals; thereafter always after ingestion of any food. Menses, which had been normal previously, now stopped. As a rule, vomiting occurred from five to thirty minutes after meals, and although it was without nausea or other warning, the patient was always able to reach a receptacle. She expressed the belief that everything eaten was vomited. Because of hunger, five meals were taken daily and the patient stated that she ate four times the usual amount of food. There was loss of weight of 30 pounds, six pounds of which had been lost within the last year.

Examination: The woman was tall and thin; her weight was 97 pounds (44 kg.) and her height was 5 feet 5 inches (165 cm.). Otherwise the examination was negative. Examination of the urine and blood, including determination of the blood urea and flocculation tests for syphilis gave normal results. Stools, analysis of gastric content and roentgenograms of the thorax and stomach were essentially normal. The basal metabolic rate was −16 per cent.

A *diagnosis* was made of functional vomiting and the patient was admitted to hospital for treatment. Treatment consisted of giving no food or fluid by mouth for two days, during which time 1,000 c.c. of 10 per cent solution of glucose and 1 per cent saline solution were given each day intravenously and in addition 1,000 c.c. of 5 per cent glucose and 4½ grains of pentobarbital sodium (nembutal) by proctoclysis. The next two days the patient was allowed small amounts of water frequently, and in addition she was given glucose intravenously as before. Thereafter the patient was allowed a piece of toast three times a day. Other dry foods were gradually added. She was dismissed on the eighth day after having been on a general diet for two days; she felt well and was very grateful.

Case 2—An unmarried woman aged twenty-three years came to this Clinic, June 25, 1934, because of vomiting of six months' duration. Significant in the history was the fact that at seventeen years of age she had begun working long hours under high tension in a factory. When twenty years of age, thyroidectomy had been performed elsewhere because of "choking spells", characterized by a lump in the throat and loss of emotional control. By this operation, relief from these choking spells was obtained but the patient never regained her strength. Thereafter fatigue became an outstanding symptom but work was continued. At this time, epigastric distress developed after eating, which distress was occasionally relieved by vomiting; after the age of twenty-one, the patient not infrequently vomited following meals. For six months before coming to this Clinic vomiting occurred after every meal. Loss of weight was from 160 to 100 pounds (72 to 45 kg.). Aside from administration of nerve tonics, treatment had not been given. Two weeks before the woman came to this Clinic, the vomiting had become much worse and the patient stated that everything eaten was vomited: "If I vomited a small amount everything would follow, even against my will."

Physical examination revealed a thin woman, 5 feet 3 inches (157.5 cm.) tall, weighing 99 pounds (45 kg.). There were no physical abnormalities. Laboratory studies of the urine and blood, flocculation tests for syphilis, analysis of gastric content and roentgenologic observation of the thorax and stomach were essentially normal. The basal metabolic rate was −15 per cent.

A diagnosis was made of functional vomiting and the patient was admitted to the hospital for treatment. This treatment was essentially similar to that reported in Case 1. However, after one week, the appetite was stimulated with insulin and the daily calorie intake of the patient was 3,000. She took this amount of food without difficulty and gained 6 pounds (2.7 kg.) during the two weeks' stay in the hospital.

Case 3—A woman of thirty-three years came to this Clinic, June 20, 1934, because of vomiting of one month's duration. At twenty-one years of age, vomiting without nausea or pain had begun to occur at irregular intervals. The patient stated that she vomited easily. When twenty-six years of age, the vomiting had been so marked that very few meals had been retained. Following three months of vomiting, gastro-enterostomy had been performed elsewhere for what was presumed to be pyloric obstruction. Practically complete relief was obtained for five years, although vomiting always reappeared with fatigue. In January, 1934, the patient came to this Clinic because of vomiting since September, 1933. Gastro-enterostomy apparently had not helped her.

The gastro-enterostomy was disconnected surgically January 27, 1934. Exploration of the stomach and duodenum revealed them to be normal. After convalescence the patient's course was satisfactory and she resumed a normal life. However, in May, 1934, she became fatigued and worried over the illness of her father. As a result, vomiting recurred, first of small amounts several times daily and thereafter of practically everything ingested. The usual sequence of events was pain in the back of the neck, belching, followed by sour eructations, and finally vomiting.

Physical examination gave essentially negative results. The weight was 10 pounds (4.5 kg.) below normal. Laboratory studies of the blood and urine, analysis of gastric content and roentgenologic studies of the stomach were normal. The basal metabolic rate was −18 per cent.

A *diagnosis* of functional vomiting was made. The patient was admitted directly to the hospital for treatment, which was essentially similar to that given in the first two cases. The response was slightly slow, as the patient was easily upset by many details, such as the noise of a fan in the room. However, she rapidly regained strength and was able to eat a general diet, although she vomited occasionally. Desiccated thyroid gland was used to elevate the basal metabolic rate, but otherwise had no apparent effect on the clinical course.

DIFFERENTIAL DIAGNOSIS

The diagnosis of functional vomiting usually can be made from the clinical history and the general appearance and manner of the patient. Psychoneurotic stigmas may not be outstanding, but if they are lacking, the clinical features already mentioned lead one to suspect the diagnosis. The possible occurrence of organic diseases among psychoneurotic individuals must not be forgotten.

The differential diagnosis requires exclusion of those diseases of the digestive tract in which vomiting or regurgitation may occur, namely, cardiospasm, pylorospasm, gastric and duodenal ulcer, carcinoma of the stomach, and so forth. Exclusion of these lesions is relatively easy and depends, in particular, on evaluation of an adequate history and roentgenologic observation. More important is exclusion of organic diseases elsewhere than in the digestive tract. These may mimic functional vomiting and lead the clinician astray. Among such conditions should be mentioned pregnancy, Addison's disease, hyperthyroidism with crisis; organic disease of the nerv-

ous system, particularly brain tumor with increased intracranial pressure; gastric crisis, uremic states, and so forth.

The astute clinician will rarely be misled if he pays attention to the clinical features, neurotic stigmas, negative examination and duration of vomiting.

TREATMENT

The treatment of functional vomiting is relatively easy if the patient can be hospitalized, but countless pitfalls must be avoided.

Certain principles which apply to the treatment of any neurotic patient must be carefully observed. In other words, the patient must have the confidence of his physician, should be under the care of one physician and not several, and should be separated as far as possible from the usual environment, including overzealous relatives and friends. The principles which Weir Mitchell enumerated for "rest cure" are well worth considering in these cases. Finally, if possible, the background for the development of the vomiting should be ascertained. This may be due to one of several types of psychic trauma, to nervous exhaustion or to some apparently insignificant incident.

Psychotherapy is of tremendous importance in the treatment of these patients. The reassurance that goes with complete confidence of the patient in the ability of his physician to exclude organic disease and to gain eventual success by the treatment is the keystone of all therapeutic efforts of functional vomiting.

So far as the actual physical treatment is concerned this has consisted of complete rest of the stomach and sedatives. In this manner the number of stimuli which reach the vomiting center is decreased. The psychic effect of taking no water or food by mouth is tremendous and is often a powerful club in the hand of the physician. Fluids are supplied by proctoclysis and intravenous injections of solutions containing salt and glucose to prevent thirst and ketosis. As a rule the patient soon tires of this treatment. Another weapon for the physician to use in overcoming the patient's resistance is to recommend complete rest in bed.

We have used sedatives in moderately large doses in the form of pentobarbital sodium (nembutal), by rectum, to reduce the general reactivity of the patient and also to reduce the irritability of the vomiting center and other centers.

After a period of two to four days on such management the patient usually tires of his predicament and becomes thirsty or hungry. It is beneficial to wait until the patient asks for food or water before supplying them. Then small amounts of water may be given every hour or half hour for a day or two. When food is supplied, it should be given in very small amounts and it should be dry, solid food, such as toast, cereal and so forth, because such foods produce greater peristaltic action than do liquid foods and are more difficult to vomit. No fluids should be allowed until two hours after ingestion of food, and then only in small amounts such as 15 to 30 c.c. at a time. If the patient retains food, the program for intravenous and rectal administration of fluid and sedatives can be gradually relaxed. The intake of food should be largely gauged by the desire of the patient. Whenever the patient suggests that vomiting may recur, she should be reminded that the previous program will be instituted again, and that aspirations of the stomach by tube will be undertaken to see just what is in the stomach. This will usually control the situation.

With continuance of this program the patient will soon be eating well of a dry diet, with fluids after meals only. Reward for good behavior, and punishment for relapse, work splendidly in the management of these cases. Rehabilitation should be gradual. The physician must be firm and if necessary uncompromising. In some cases in which difficulty is encountered, additional aid may be had during the period of recovery from the use of (1) insulin to stimulate the appetite, (2) feeding by tube, (3) elevation of the basal metabolic rate if it is low, and (4) occasional gastric lavage.

PROGNOSIS

The immediate prognosis in these cases is usually good. The rapidity with which progress is made, and the ultimate prognosis, depend almost entirely on the degree and extent of the abnormal psychiatric state of these patients. Those who do not display marked psychoneurosis or in whom psychotic changes are not advanced, generally do well. Also they get along satisfactorily if the vomiting is largely a habit or if the underlying cause may be removed without too great a struggle.

SUMMARY

The diagnosis of functional vomiting is made on the general appearance and manner of the patient, the negative examination, and the clinical features and long duration of the vomiting.

A method of treatment is described which proved successful in functional vomiting. Report of three of these cases is made.

The essential features in this treatment are hospitalization, complete rest of the stomach, and sedatives, with reassurance of the patient of the absence of organic disease and gradual rehabilitation.

The Relation of Anemia to Surgical Diseases of the Gall Bladder*

By

RALPH A. KORDENAT, M.D.
CHICAGO, ILLINOIS

THE liver long has been recognized as being vitally concerned with erythropoietic function. The close anatomical, embryological and physiological relationship between the liver, gall bladder and stomach should lead one to investigate these organs to determine any possible correlation between their pathological changes and an anemic state. The numerous instances of anemia in a series of 116 cases of surgically proven derangements of the gall bladder, reported herewith, are so striking that it does not seem a coincidence. Several pernicious-like anemias were noted in this series.

Meltier[1] compared the pathological findings of the liver of 20 patients previously afflicted with pernicious anemia who died without treatment, and those of five patients who had received treatment, but who died from intercurrent disease. He found a marked enlargement of the Kupffer cells in all 20 untreated cases. There was an increased cytoplasm and swelling of the nucleus with phagocytosis of red blood cells. These cells also contained the yellowish-brown pigment of hemosiderin. The Kupffer cells found in the livers of those who had received treatment, but who died from other causes, were normal and only occasionally enlarged and more often small and slender. The observer believes a slight enlargement to be a response of the reticulo-endothelial system to infection. Fatty degeneration was seen, but was not extensive. Siderosis was equivalent to that present during a relapse or in early cases of remission. In the untreated cases, siderosis was marked in the liver cells and moderate in the Kupffer cells. There was a desquamation of Kupffer cells with phagocytosis of red cells, but not more so than in other types of anemia or in infections. In contrast to Piney's observations, Meltier found no evidences of blood formation in the liver. Megaloblasts occurred freely in the sinusoids of the liver of patients who died during a relapse. Warthin[2] also doubted that red blood cell formation occurs elsewhere than in bone marrow. He believed that the presence of nucleated red cells in liver sinuses could be explained by their presence in the circulating blood.

Additional historical data which leads one to investigate clinically the relation of anemias to infection of the biliary tract is that of the detoxifying function of the liver. Opie[3] after reviewing numerous studies concluded that the liver by means of its peculiar endothelium not only removes bacteria and other injurious substances from the blood of the portal circulation, preventing them from entering the general circulation, but in so doing causes some destruction of the liver tissue itself. If this occurs over a long period of time there must undoubtedly be an alteration in the erythropoietic mechanism, as far as the liver is concerned. Long-continued infections of the liver also will lower the fibrinogen content.

Mann[4] noted experimentally that hepatectomized dogs have a reduced immunity to certain poisons, in addition to the hypoglycemia and changes in protein metabolism. A diseased liver could likewise permit micro-organisms and obnoxious material, ordinarily removed by the Kupffer cells and excreted by the bile, to enter the general circulation and gradually but surely injure the bone marrow. The reticulo-endothelial system of the liver, aside from other functions, is concerned in the phagocytosis of dying erythrocytes and bile formation. It has been shown that the liver produces a large share of bilirubin. The site of bilirubin formation has been rather vague, but it is now quite generally believed that the entire recticulo-endothelial system enters into its formation, particularly that of the liver, spleen, bone marrow and lymph-nodes. In a grossly deranged liver then, evidenced by an obstructive jaundice, the injured liver cells will not permit the normally-formed bilirubin to be excreted, but it is reabsorbed as described by McNee.[5] The marked beneficial effect of liver extract in instances of liver damage of a lesser degree than in pernicious anemia would seem to substantiate these experimental observations.

Many observers have shown[6] that the liver exerts a striking effect upon the regeneration of

*From the Department of Surgery, University of Illinois College of Medicine, Chicago.
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hemoglobin. Whipple[7] has beautifully demonstrated a variation in the value of different livers when used for its hemoglobin-production factors. Fish liver practically is inert in its effect as a producer of hemoglobin, while the liver of warm-blooded animals contained those factors. In atrophic human livers there is a lower content of hemoglobin-production factors. In livers of humans dying of fulminant infections, the ratio is also low, while this factor in the livers of humans with a thyrotoxiosis varied widely. The values are low in diabetes, a disease in which there is frequently a combined derangement of both pancreatic and liver function. The antianemic principle of human livers has been further studied by Ivy and his associates.[8] They made separate extracts from livers of two individuals who died of pernicious anemia, one who had been treated and one who had not. They found no response where the liver extract of the untreated case was used but obtained a favorable response where the liver extract of the treated case was used. This led them to conclude that the specific antianemic substance in liver administered to pernicious anemia patients is stored by the liver. It is conceivable that this substance might be lacking in whole or in part in those partially damaged livers associated with definitely diseased gall bladders.

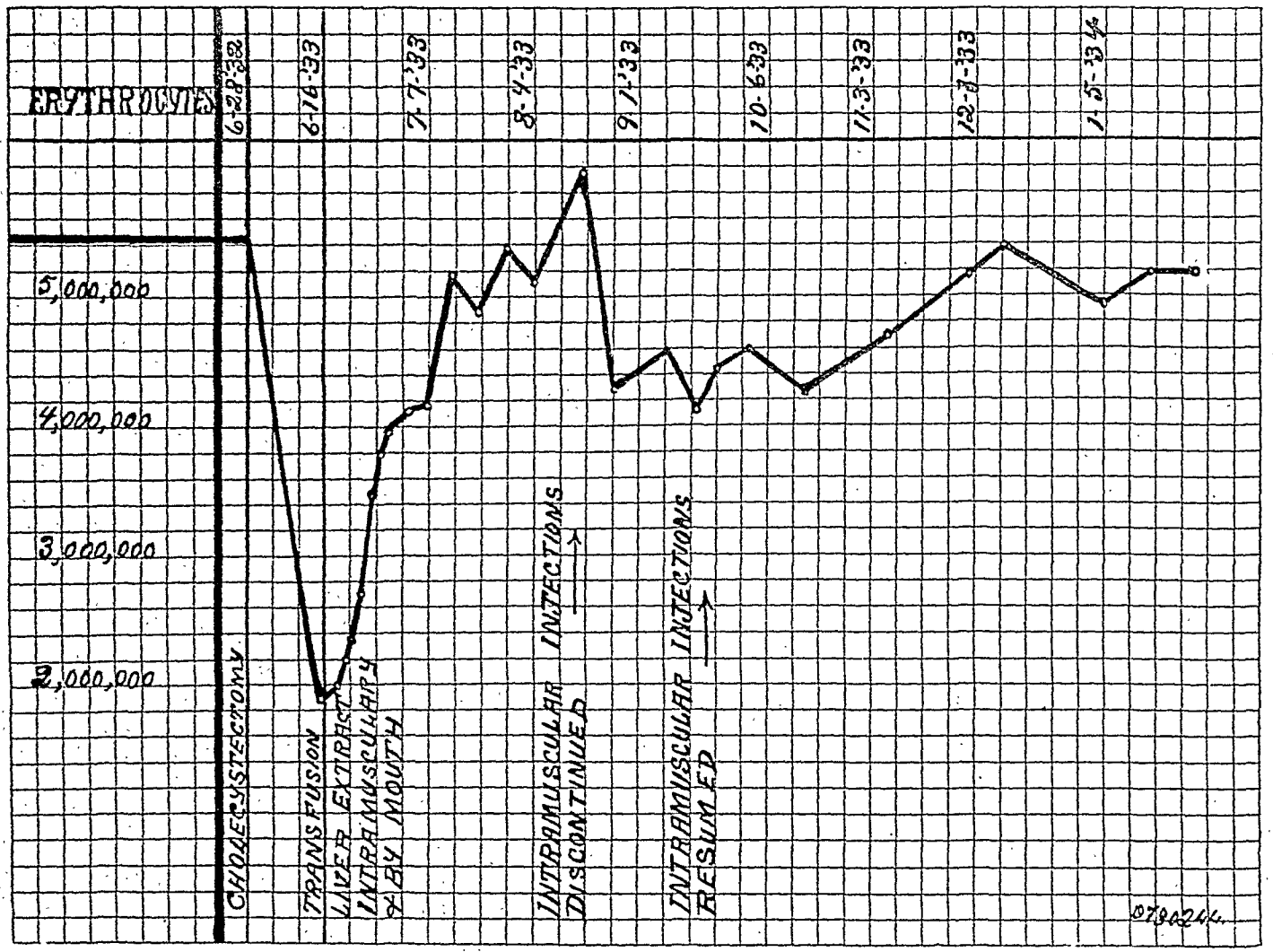
Dixon[9] observed the inability of the haemotopoietic organs to keep pace with the anemia in an instance of primary idiopathic abscess of the liver.

Moschcowitz[10] in discussing hypoproteinemia calls attention to the low blood protein that is fairly constant in pernicious anemia. It is well known that the liver is active in protein metabolism.

The close relation of liver function to the anemias of pregnancy is well known. Mussey[11] found evidences of toxicity in 51 of 82 cases of anemia of pregnancy, though was unable to determine the nature of these toxic factors.

Whipple[12] believes the liver to be largely concerned with the complex pigment metabolism of the body. He believes that anemias are not due to toxins, but to a lack of something, especially in pernicious anemia. He believes that pernicious anemia is due to a lack of a stroma-building mate-

Chart 1—Erythrocyte count in Anemia following Biliary Tract Infection.



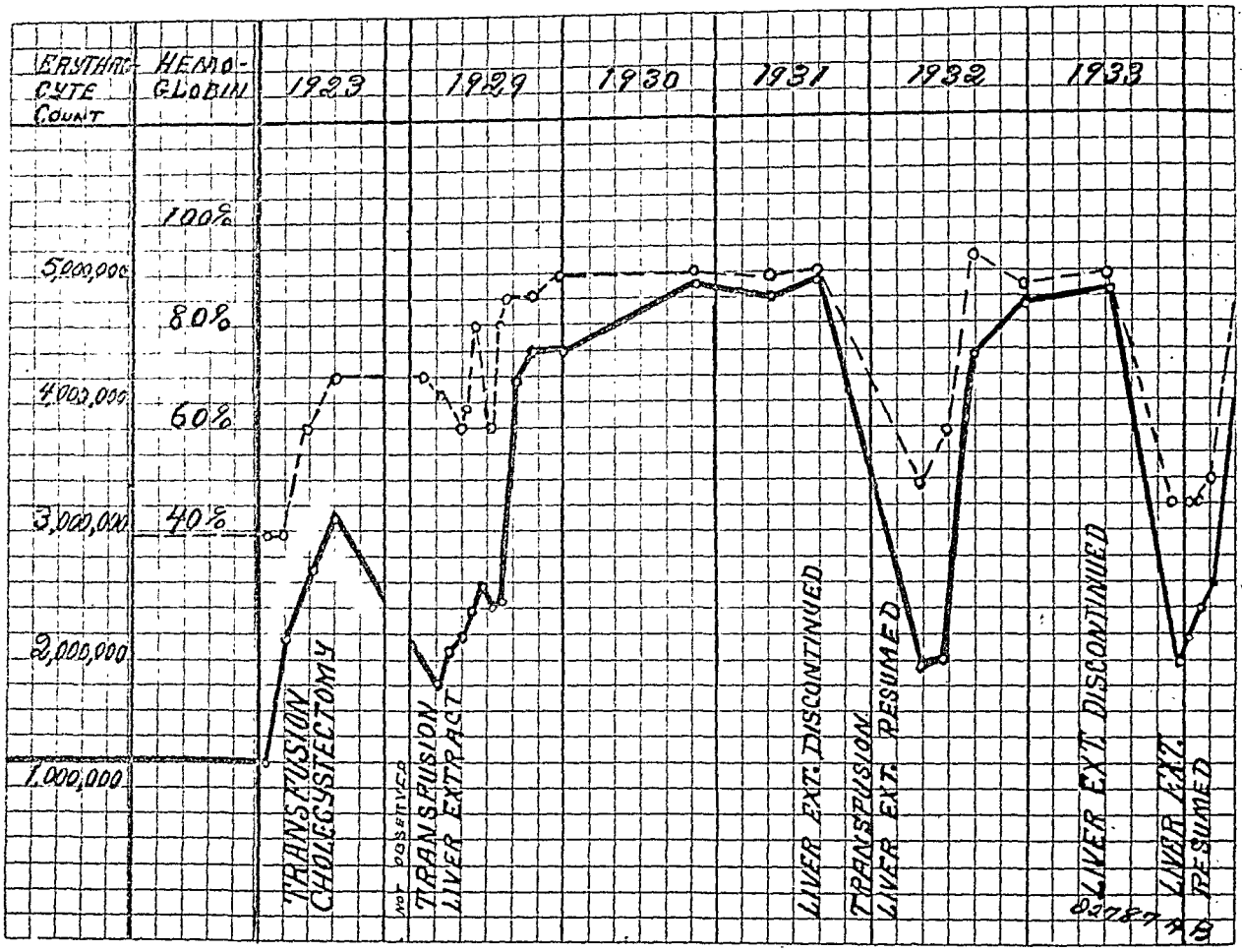


Chart 2—Erythrocyte and Hemoglobin curve in Anemia following Biliary Tract Infection.

rial and an excess of pigment and pigment-building material. It has been suggested that, while it may be difficult to demonstrate any toxic substance as a possible etiological factor of such anemia, advocates of a toxic origin have, in their argument, favorable evidence that the toxins are the result of deranged metabolism due to malfunction of the erythropoietic organs. The liver and stomach are outstanding among these.

There is considerable evidence that anemias occurring in experimental jaundice are due in a great part to defective blood formation and not to excess hemolysis. Jordon and Green[13] have shown that the concentration of bile salts necessary to produce hemolysis *in vitro* does not occur in chemical or experimental jaundice. Following a preliminary rise in bile salts, there occurred a gradual fall after obstruction of the common bile duct in animal. The urinary excretion of bile acids in obstructive jaundice also shows a similar fall. If anemia were due to excessive bile, it would be greatest at the height of bile concentration. Furthermore, blood serum has a protective action against hemolytic agents. Jordon and Green ligated the common bile ducts of dogs and found a progressive fall in hemoglobin. The anemia which was produced usually remained stationary at a moderately low level. They noted the same blood picture in dogs with biliary fistulae.

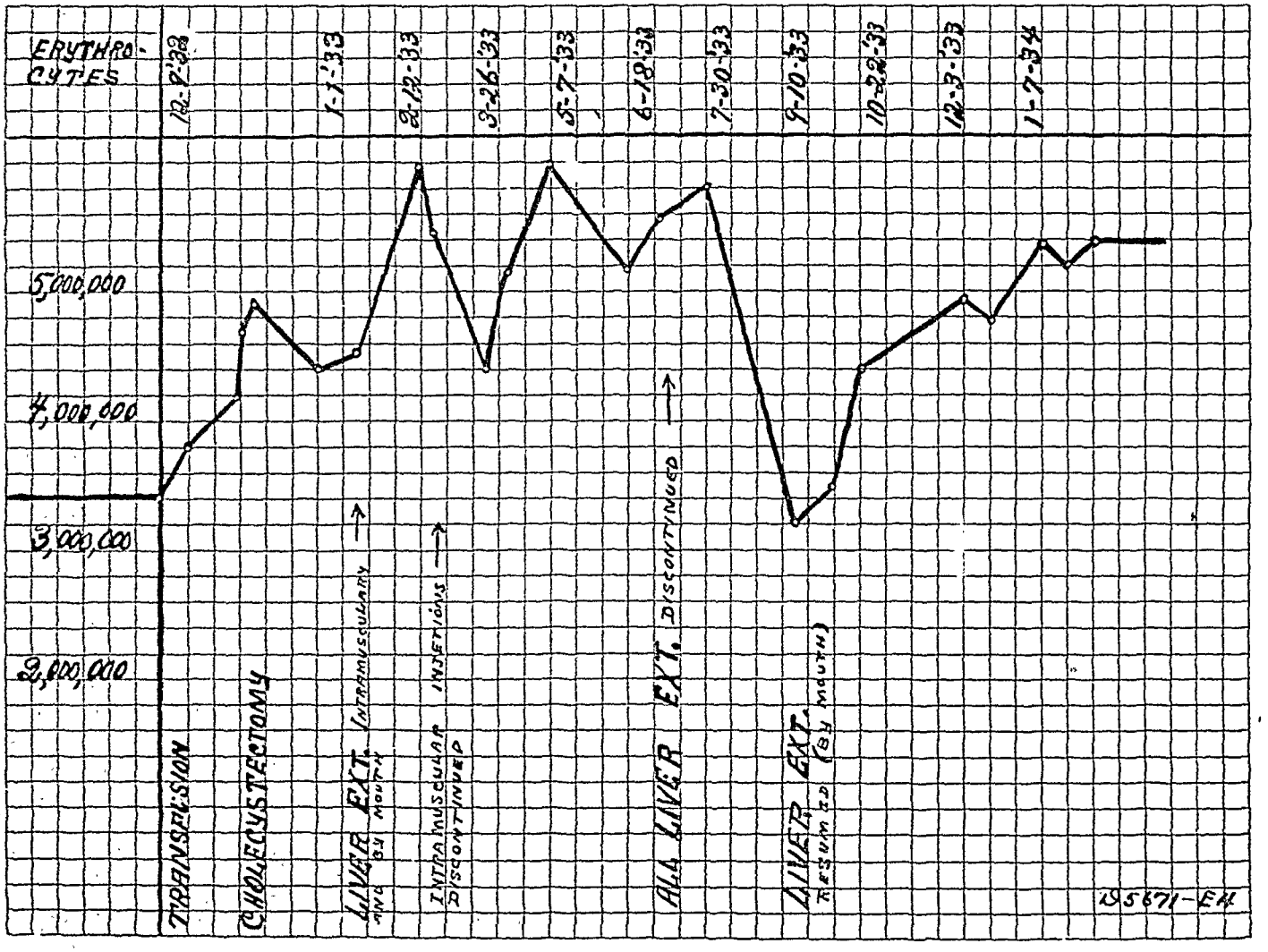
The beneficial effects of feeding bile in the treatment of anemias due to biliary fistula, indicates the value of bile salts in stimulating certain "lacking" factors necessary for the proper erythropoiesis where liver extract alone is of no value.[14] The failure of liver extract to influence bile pigment formation has been demonstrated experimentally by Kim.[15] He fed liver extract to dogs with biliary fistulae and noticed no influence on the output of bile or bile pigment. Sharp[16] has called attention to the probability of defective liver function as well as abnormal gastric conditions in persons predisposed to pernicious anemia.

Minot[17] has proven conclusively that the reaction of the reticulocytes in pernicious anemia is apparently due to specific action of the effective material contained in liver, kidney and other tissue. This potent substance can produce a similar result in other conditions, but not in ordinary

secondary anemia. He believes that in other anemias in which liver extract has a favorable influence on both reticulocyte response and erythrocyte formation there is a distorted blood formation that approaches the character of pernicious anemia. In pernicious anemia, the specific substance of the liver promotes growth of the primative cells that crowd the bone marrow by allowing better maturation and transforms a megaloblastic marrow into a normoblastic one. This effective material might well be lacking in smaller amounts in the defective livers seen associated with gall bladder disease.

One is truly impressed by Krumbhaar's[15] views on the active processes in pernicious anemia. He has advanced the belief that pernicious anemia might well be due to an intestinal noxious agent somewhat associated with achlorhydria and absorbed by the portal circulation. There it may upset that organ's hypothetical relationship to hemopoiesis, by hindering it in furnishing a necessary ingredient, with the result that inefficient erythrocytes prematurely are sent into the blood stream. In spite of the bone marrow hyperplasia an insufficient number of inefficient erythrocytes are turned out to be destroyed in excessive numbers by the spleen which is stimulated to overactivity by the passage of the noxious agent through that organ. Whipple has contended that pernicious anemia is a deficiency disease where there is a deficiency of the materials that build up the stroma of the cells. Krumbhaar, by removal of dog's spleens or by diverting the splenic blood from the liver, produced a transient anemia which led him to believe that the normal spleen secreted something into the blood which, after its passage through the liver, exerted a stimulating effect on the erythropoietic function of the bone marrow. He pictures the removal of a spleen that is diseased to have the opposite effect on the blood picture. The spleen, being a complex organ of several functions, may have some other influence, while in a state of hypersplenism as in pernicious anemia, in preventing the liver from exerting its maturating effect on the erythroblasts, a defect supplied by liver extract.

Chart 3—Erythrocyte count in Anemia following Biliary Tract Infection.



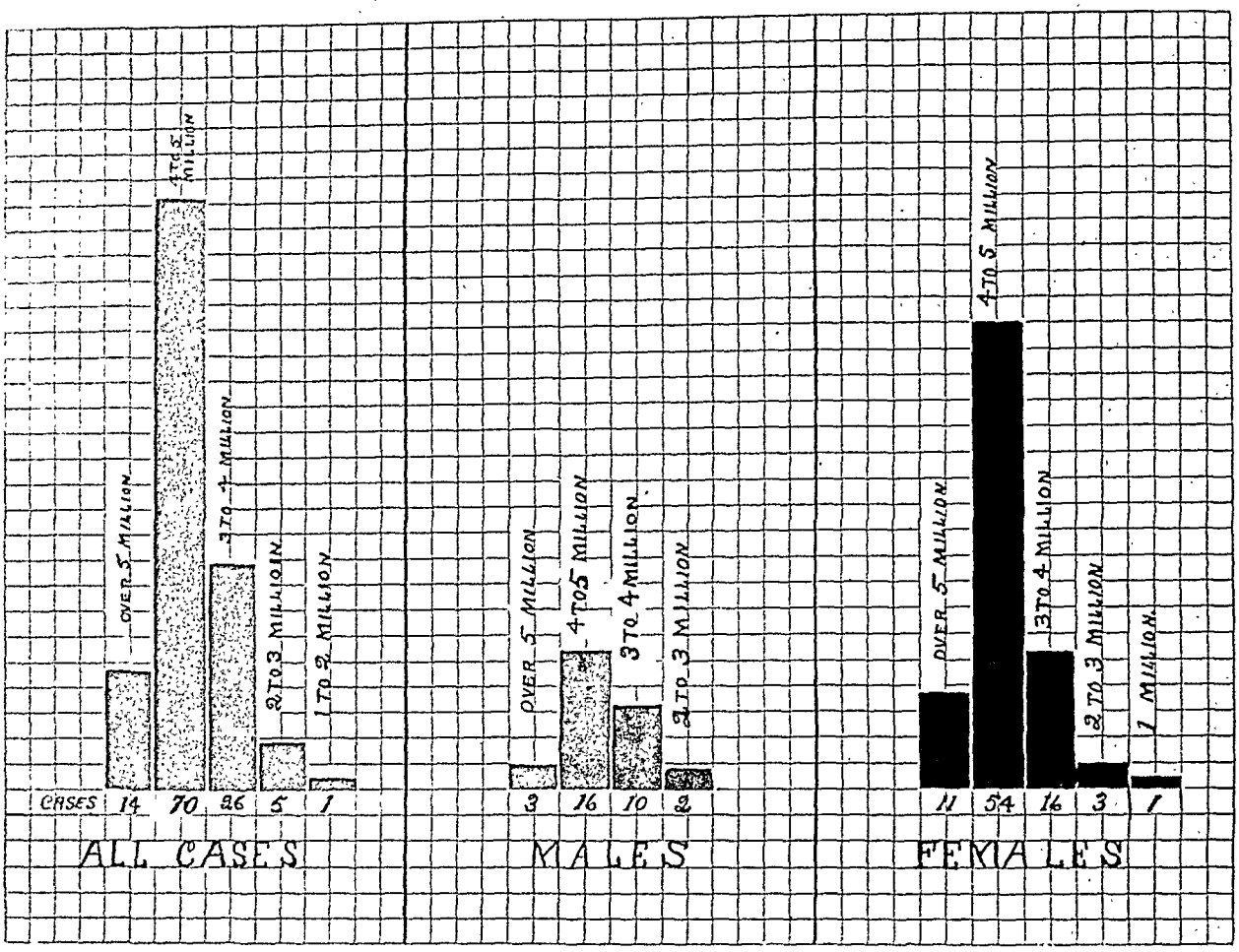


Chart 4—Erythrocyte counts in 116 cases of Surgical Diseases of the gall bladder.

MATERIALS AND METHODS

The blood pictures of 116 patients who had undergone operations either for drainage or removal of the gall bladder were studied. Of these 79 were operated upon by the surgical staff of the Illinois Research and Educational Hospital. The series represents the average type of such cases. Only those where complete blood observations were made were studied.

There were three deaths of this series of 116 patients. The causes of death were (1) broncho-pneumonia (male, age 45), erythrocyte count, 2,280,000; (2) broncho-pneumonia (female, age 41), erythrocyte count, 4,848,000; (3) carcinoma of head of pancreas (male, age 70), erythrocyte count, 3,000,000. The *average erythrocyte count* of *fatal* cases was 3,376,000. The *average erythrocyte count* of *all females* was 4,115,341, while that of *all males* was 4,183,600. There were 14 patients (three males and 11 females) with red blood counts over 5,000,000 (see Chart No. 1); 26 patients (10 males and 16 females) with counts between 3,000,000 and 4,000,000; five patients (two males and three females) with counts between two and three million; one patient (female) whose whole count was between one and two million. The lowest count was 1,250,000 (reported in detail) and the highest was 5,500,000 (female).

The histories reviewed herewith are those of cases from four hospitals. The hemoglobin estimations were made with various instruments, using various methods. Necessarily there is, therefore, some discrepancy in the value of the hemoglobin determination. The average hemoglobin of all females was 74.6 per cent and of all males was 76 per cent. The hemoglobin estimations varied from 40 to 95 per cent, while in some instances was not estimated at all.

The determinations of the *carbon dioxide combining power, non-protein nitrogen, blood sugar, gastric analysis* and *icterus index* were not made in all cases. The averages given herewith represent those of the various determinations found in those histories of cases where this work was actually required. The *carbon dioxide combining power* did not vary greatly from normal. The average was 56.6. The *icterus index* varied from

the lowest incidence of three to the highest of 175. The *blood sugar* was high in many instances, though low in some. The highest was 154 mg. per 100 c.c. of blood and the lowest was 87 mg. per 100 c.c. of blood. The average blood sugar for females was 121 mg. and for males was 93.3. The *non-protein nitrogen* was variable. The lowest was 24 mg. per 100 c.c. blood and highest was 115 mg. per 100 c.c. blood with an average of all cases of 42.1. The average for females was 56.3 mg. and higher than males (33 mg.). This was probably incidental. There seemed to be no relation between the erythrocyte count and the non-protein nitrogen determinations of this series.

The average analysis of *gastric contents* of females was: total acidity 36.7°, combined 18.4°, and free acidity 18.2°. There was no free acid in five instances among the female patients. The red blood counts were low in all those instances where there was no free acid. They were as follows: 1,230,000 to 1,840,000; 3,360,000 to 4,350,000; 4,650,000, with an average of 3,686,000.

Syphilis can be excluded as an etiological factor of the anemias of this series. In only one instance was the Wassermann reaction positive (1 plus).

CASE HISTORIES

Case 1—Miss L. L., aged 65, of Irish descent, was admitted to St. Joseph's Hospital, June 16, 1933, because of extreme weakness and "sore tongue". On June 29, 1932, her gall bladder was removed. The gall bladder contained a number of stones. The wall was thickened and fibrotic. She experienced no difficulty until December, 1932, when she began to notice a gradually increasing weakness. On June 29, 1933, there was some emaciation and extreme pallor of skin. The tongue was somewhat swollen, very smooth, dry and a small marginal ulcer was present. X-ray examination showed no pathology in stomach or duodenum. Colon was extremely spastic. Examination of gastric contents revealed an absence of free hydrochloric acid. Total acidity 12°. The erythrocyte count was 2,050,000. Macrocytosis was marked and blood plasma tinged to a golden brown. Vandenberg tests indicated bile pigments in plasma. There was a marked variety in size of the cells, poikilocytosis, basophilic stippling and an occasional normoblast. Hemoglobin, 55 per cent. Leucocyte count, 3,200.

Five hundred c.c. of whole unmodified blood were transfused on June 17, 1933; 10 c.c. doses of liver extract were then given orally and intramuscularly for two weeks. Intramuscular injections were later given at weekly intervals. There was a constant improvement in the erythrocyte count, normoblasts became more numerous. The reticulocyte response was pronounced. (See Chart 2.) Four months later the intramuscular injections of liver extract were discontinued. The erythrocyte count then dropped from 5,800,000 to 4,200,000 in about two weeks' time. Weekly injections of 2 c.c. of liver extract were again given and the blood returned to normal. The cells then showed no abnormalities.

Case 2—Mrs. A. B., aged 62 years, was first seen by me on July 18, 1923, for the relief of weakness, palpitation, pain in upper right abdominal quadrant, nausea and vomiting. She was extremely pale and the skin was of a lemon yellow color. There was tenderness over the region of the gall bladder; there was no jaundice. The tongue was smooth, dry and without ulcerations. Laboratory examination revealed an erythrocyte count of 1,230,000. Hemoglobin, 40 per cent; color index, 1.4; leucocyte count, 3,150. The red cells were variable in size and there were numerous macrocytes. Normoblasts were occasionally seen. Poikilocytes were numerous and some polychromatophilia were observed. No stippling cells were noted, though neuclear remnants were found in the form of Howell-Jolly bodies. The urine was negative. Gastric analysis showed a total acidity of 8°, with no free hydrochloric acid.

On July 20, 1923, 600 c.c. of whole blood were transfused and cholecystectomy done. The distended gall bladder with its atrophic wall, resembled a wet parchment bag, filled with gravel. The liver was smooth with a mottled appearance. The spleen was somewhat larger than normal. The patient improved and on August 25, 1923, the erythrocyte count was 2,730,000. Hemoglobin, 60 per cent, and color index, 1.1. April 2, 1929, she was again admitted to the hospital with similar complaints. At this time the erythrocyte count was 1,670,000. Hemoglobin, 67 per cent; blood sugar, 132.4 per 100 c.c. Non-protein nitrogen was 35.9 mg. per 100 c.c. of blood. The carbon dioxide combining power was 62 volume per cent. The urine was negative. Gastric analysis revealed a total acidity of 5°, with no free hydrochloric acid. At this time she was again given a whole blood transfusion and in addition liver extract by mouth. The resultant improvement was more phenomenal because of added benefit of the liver extract. The erythrocyte count rose to normal. There was a spectacular reticulocyte response. Normoblasts increased and the red cells later appeared normal. Small daily doses of liver extract were given by mouth in addition to a diet including liver, kidney and calves' brains, until December, 1932. At this time the patient tiring of her treatment, discontinued her diet and all medication. There was a rapid decline in the erythrocyte count and progressive increase in weakness. The erythrocytes had dropped to 2,030,000. Hemoglobin, 58 per cent. Because of the extreme weakness, transfusion was again performed, the administration of liver extract resumed, with a third spectacular rise in the red blood cell count and hemoglobin. The reticulocytes increased, mature red cells became more uniform in size and shape, normoblasts increased, neuclear remnants were less noticeable, the general health and blood picture continued to remain normal to date.

Case 3—Mrs. E. H., aged 55 years, was admitted to St. Joseph's Hospital, December 13, 1932, because of intermittent pain in the right upper abdominal quadrant, that radiated to the right scapular region, weakness, eructations of gas and constipation. There was no evidence of icterus. The erythrocyte count was 3,860,000; hemoglobin, 84 units (105 per cent); leucocytes, 5,900. There was a marked anisocytosis with many macrocytes. Polymorphonuclear neutrophiles numbered 66 per cent; small lymphocytes, 28 per cent; large lymphocytes, 3 per cent; monocytes, 3 per cent. The electrocardiograph findings showed a depression of the R. T. segment in Leads I and II, deep Q wave and slurred R wave in Lead III; suggestive of myocardial damage.

X-ray examination showed a gall bladder of poor contracting power and shadows of subnormal densities suggestive of calculi. The colon filled readily, showing no filling defects but was smooth and without normal peristalsis. There was an incompetent ileocaecal valve.

The patient was given 600 c.c. of whole blood and cholecystectomy done under local and ethylene anesthesia. The gall bladder was distended and contained several stones. The wall was characteristic of a chronic cholecystitis. The erythrocyte count rose steadily to nearly 5,000,000 (see Chart 4), and the cellular elements again appeared normal. A month later there was a drop in the erythrocyte count to 4,200,000 and at this time macrocytes, and pessary forms were numerous, though at no time were poikilocytes or macrocytes seen, though there was a definite scarcity of reticulocytes. Liver extract (Lilly's 343) was now given intramuscularly and by mouth. This was followed by immediate improvement in the blood picture as well as an improvement in the patient's weight and

general condition. Six months later (July, 1933) the liver therapy was discontinued. There followed a drop in the erythrocyte count to 3,200,000. Upon resuming the liver therapy improvement again followed. It now requires a minimum dose of one capsule (Lilly's Lextron) every two days to maintain a normal blood count.

COMMENT

Blood Sugar: The blood sugar determinations were made upon patients while under preparation for surgical treatment and would naturally be in contrast to those made in other circumstances. These observations are of interest, especially in view of Mann's study of hepectomized dogs. He has demonstrated the importance of the liver as the sole regulating mechanism of blood sugar. Though the average blood sugar in six instances was 109.1 mg. per 100 c.c. of blood, it was high in the majority of cases. Having in mind the close relationship of diabetes with infections of the liver and biliary tract, these observations of a rather low tolerance suggest that relationship more strongly. It impresses one at least of an associated liver disfunction accompanying many surgical diseases of the gall bladder.

Non-Protein Nitrogen: Determinations were high in 12 observed cases with an average of all cases of 42.1 mg. per 100 c.c. of blood. The kidney is believed to be a great regulator of the nitrogenous composition of the blood. The liver, however, is believed to be necessary for the diaminization of amino acids, synthesis of urea and phases of destruction of uric acid in protein and purin metabolism. Consistently high non-protein nitrogen in this series may be considered as evidence of blood cell destruction. Moschcowitz[10] believes that hypoproteinemia may result from (1) loss of proteins through the kidneys, the intestinal tract or direct blood loss; (2) by deficient formation or destruction of proteins, and (3) by insufficient intake of proteins as in famines or war edema. He has also called attention to the fairly constant low-blood protein in pernicious anemia. No definite conclusions were drawn from the high non-protein determinations. The determinations were made only in 12 instances and the majority of these were elderly individuals.

The Carbon Dioxide Combining Power, indicating the degree of acidosis, was determined too infrequently to give a representative series. In those recorded, however, it varied very little from the accepted normal.

The Analysis of Gastric Contents proved interesting and would seem to indicate a clinical confirmation of the experimental work of Conner,[19] Castle,[20] Fouts and Zerfas,[21] Sharp,[16] and others. In the 20 instances where gastric analyses were made the average total acidity was 29.8 degrees; the average combined 17 degrees and the average free acid was 12.8.

In each instance in this series of 20 cases where the free acidity was below normal, the erythrocyte count was below 4,500,000. In five instances there was no free acid, and in these the erythrocyte counts ranged from 1,200,000 to 4,650,000 with an average of 3,072,000.

Cheney[22] studied the morphology of erythrocytes in hepatic disease and concluded that these anemias are clearly separate from other secondary anemias. He found the red cells larger and frequently contained sufficient hemoglobin to give a color index of more than 1. In many of the cases reported herewith macrocytosis was seen, often in the extreme degree. In three instances shown graphically by Charts 2, 3 and 4, macrocytes were seen over a variable period, but less noticeable at the time the erythrocyte count approached normal.

OBSERVATIONS IN 25 INSTANCES OF SURGERY OF THE BILIARY TRACT, WHERE THE ERYTHROCYTE COUNT WAS LESS THAN FOUR MILLION

	High	Low	Ave.	Normal
Blood sugar in mg. per 100 c.c.	154	87	109.1	80–120
N.P.N. in mg. per 100 c.c.	115	24	42.1	25–40
CO_2 combining power in vol. %	65	48	56.6	50–75
Gastric total	52°	5°	29.8°	75–100°
Analysis Comb.	24°	5°	17.°	25°
In degrees	30°	5°	12.8°	1–25°
Icterus index	173	3	62	6

Though one cannot, in this series of cases, determine the incidence of the liver damage that was associated with the definite pathology of the gall bladder, it is reasonable to suppose in the light of the numerous instances of anemia, that a very close relationship undoubtedly existed between the anemia and the liver disfunction. That liver disfunction may be associated with certain anemias has been generally accepted. The question arises whether the liver damage is primary or secondary to those diseases of the gall bladder where biliary calculi are the predominating factors early in the course of disease as in cases here reported. Judd found it difficult to obtain satisfactory bacteriological cultures from the gall bladder wall. He obtained 47 per cent positive cultures of the gall bladder and 27 per cent positive of pieces of liver that were separately cultured. Though he found it difficult to establish the significance of bacteria in hepatic change he concluded that hepatitis or cholangitis occurred routinely in the presence of cholecystitis. Such consistent liver impairment must surely alter its maturing effect on the red corpuscles.

SUMMARY

The blood findings of 116 instances of gall bladder diseases are presented. They suggest a close relationship between the anemia observed and liver disfunction.

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ABSTRACTS

STEIN, IRVING F.

Oxygen Pneumoperitoneum in the Diagnosis and Treatment of Tuberculosis of the Genitalia, Intestine and Peritoneum. Surgery, Gynecology and Obstetrics. Vol. LVIII, No. 3, March, 1934, pp. 567-677.

The author, reasoning that if the therapeutic value of simple laparotomy in tuberculous peritonitis lies in the exposure of the tissues to oxygen, then it is much safer, simpler and a great economic gain to insufflate the abdominal cavity with pure oxygen by means of a needle. If no beneficial effects are noted after such treatment laparotomy may still be done, the gas having done no harm.

In the author's experience diagnostic pneumoperitoneum has been of decided value in establishing the diagnosis of tuberculous salpingitis which is the most common cause of tuberculous peritonitis. In suspected cases of pelvic tuberculosis oxygen is used in place of carbon dioxide because of therapeutic effect as well as its diagnostic value. The fallopian tubes are usually greatly thickened and tortuous so that they cast an unusually dense shadow on the roentgen film; they are usually patent. Calcium deposits may be seen in their walls. By injecting an opaque substance into the uterine cavity and the fallopian tubes their relation to a pelvic mass may be made clear.

The procedure is exceedingly simple, and differs in no way from that of transabdominal pneumoperitoneum with carbon dioxide for gynecological diagnosis. The bowels should be emptied by means of a cleansing enema. About one-half hour before, a dose of morphine sulphate should be given. The bladder should be emptied. The skin of the lower abdomen is now sterilized, and a rather firm, flexible needle, three inches in length and fitted with a stylette, is introduced through the abdominal wall. The point of introduction is usually one inch to the left of the umbilicus, and slightly below the level. The needle is held vertically between the thumb and third finger at right angles to the skin, and is introduced into the peritoneal cavity by means of pressure of the forefinger on the stylette. Three resistances are met: first, the skin, second, the aponeurosis and third, the more sensitive peritoneum. The needle is attached by means of a rubber tube to an apparatus such as is used for the Rubin patency test, and oxygen is allowed to flow in. A liter of oxygen produces little discomfort, and is usually a sufficient dose. The needle is quickly withdrawn; no dressing is required. The patient is kept flat on the X-ray table and maintained in that position to prevent "shoulder pain", which is due to the entry of gas into the right sub-diaphragmatic space. Shoulder pain, if it occurs, may be relieved by elevating the foot of the bed, or by raising the patient's hips on a pillow. Those who have used the method have repeated the insufflation in periods ranging from four days to two weeks. The author recommends weekly insufflations of about one liter each, the number of insufflations depending on the results obtained. It is recommended to keep the patient in bed for 18 to 24 hours after each insufflation.

The author cites 64 cases from the literature, and reports six additional cases, two of which represent cures of four and five years respectively. In utilizing oxygen therapy one should keep in mind that climate, good food and tonics are helpful. Surgery is indicated if the condition is complicated by a mixed infection. The author concludes that oxygen pneumoperitoneum is a safe, simple and valuable method of diagnosis and treatment of tuberculous peritonitis, which has almost escaped general notice.

Nelson M. Percy.

W. W. ROBINSON, M.D.

Extra-Bulbar or Duodenal Ulcer. South. Med. Jour., 27:759-763, September, 1934.

In a concise informative article which should be read in its entirety the author calls attention to the true duodenal ulcer—the one which occurs in the relatively fixed retroperitoneal first coil of small intestines—contrasting it to the usually recognized one occurring in the duodenal cap and comprising nine-tenths of all postpyloric ulcers.

Because of the adequate blood supply and lack of torsion in this fixed portion of the duodenum, together with the lack of acidity, the usual etiological factors of ulcer causation do not operate. Instead, duodenal stasis seems the most likely predisposing factor and this stasis when observed by X-ray examination should make one suspect the possibility of the ulcer. Clinically the usual definite symptoms of ulcer are not always present and may be replaced by those suggestive of a chronic cholecystitis. Hematemesis or tarry stools may be the dominant features. The more distal the ulcer in the duodenum the more likely is it to heal rapidly and without complications. It is suggested that more attention be given to the recognition of this type of lesion instead of limiting one's observation to the duodenal cap alone. Roentgenologic examination is, of course, the most certain means in establishing the diagnosis once the presence of the ulcer is suspected or its possibility borne in mind.

J. Duffy Hancock, Louisville, Kentucky.

SECTION VIII—*Editorial*

The editorial contributions published in this Journal represent only the opinions of their writers. Such being the case, this Journal or the American Association is in no way responsible for editorial expressions.

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

SHALL WE HAVE "STOMACH SPECIALISTS" OR INTERNISTS CERTIFIED AS GASTRO-ENTEROLOGISTS BY A QUALIFIED NATIONAL BOARD?

To those interested in research and the clinical aspects of diseases of digestion and nutrition, the decision of the National Advisory Board for the Certification of Specialists not to approve the setting up of a Board for the Certification of Gastro-Enterologists came as a surprise and a disappointment.

With the advice and under the guidance of individual members of the National Board and of the Board itself, indeed, with its approval and encouragement, for more than a year a Committee composed of men of experience, integrity and ideals (appointed by the American Gastro-Enterological Association and the Section of Gastro-Enterology and of Proctology of the American Medical Association) labored diligently and with the highest motives. On all debatable points this Committee had consulted with Members of Boards already in operation and able to exhibit records of service justifying their foundation and their continued existence.

At no little personal sacrifice of time, energy and funds, those upon whom rested the responsibility for establishing and maintaining on the highest ethical and professional plane, a National Board for the Certification of Gastro-Enterologists, brought to the 1934 Cleveland general meeting of certification boards, a constitution and by-laws of extraordinary merit. This document, submitted as the basis upon which men most experienced in the investigation and the practice of gastro-enterology proposed to establish standards and to regulate practice, by the concensus of opinion of the Members of the National Board, was admirable in all regards. In many respects it set up standards, principles and safeguards against transgression, considerably higher than did similar formulae governing certain other Boards for the Certification of Specialists thus far established and functioning. Generally, it was admitted that the Constitution and By-Laws submitted by the Board for Gastro-Enterology were excelled in scope, demands upon candidates for certification, practicability, ethical aims and ideals by the Constitution and By-Laws of no group thus far sanctioned by the National Board.

The members of the combined committee representing the gastro-enterologists — investigators, surgeons, internists—justly felt proud of what had been accomplished. Individually and collectively, they were congratulated upon their efforts by members of the National Board.

This happy state of affairs existed to within a half hour of the time set for the dinner and the annual meeting of the National Board, the representatives of various already approved and incorporated special Boards and of Boards of Specialists seeking sanction. Then, without warning, quietly it was whispered that the National Board at a previous date—time not specified—had informed the Councils of Medical Education and of Hospitals of the American Medical Association, that it (the National Board) approved of but a limited number of Special Boards—those of Gastro-Enterology and of Proctology were not included in the roster—and that, acting upon the advice of the National Board, the Association's Councils had acquiesced to the groupings made.

Such unusual and unorthodox, not to say unfair and discriminatory action, seemed impossible of belief. Had not the National Board's Members constantly been in the closest contact with the Committee of gastro-enterology during the preceding year? Had they not abundantly given advice and encouragement (as can be substantiated by letters, telegrams, etc.)? Even to within a few minutes of going in to dinner, had not important Members of the National Board approved of and suggested certain minor changes in the gastro-enterology Board's By-Laws?

Although the Gastro-Enterological Committee was given a hearing at the meeting of the National Board held following dinner, from the opening of the discussion, it was evident that (a) whatever might be the arguments advanced, they would carry no weight; (b) the National Board's membership was divided in its attitude towards the proposed Board of Gastro-Enterology, and (c) that, through influence, bias and "back-stage" pressure, certain men, potent groups and institutions already had served notice that their edicts must be enforced or dire "political" consequences would follow. The meeting ended abruptly at an early hour with the Gastro-Enterologists' pleas for reconsideration completely ignored.

With rare tolerance and restraint, the subsequent events at the 1934 Cleveland Session have been placed on record by Dr. A. F. R. Andresen, of Brooklyn.* In summary, the Gastro-Enterologists believed that a misunderstanding of motives

*Editorial Section, *American Journal of Digestive Diseases and Nutrition*, p. 595; October, 1934.

and procedure had occurred; they felt strongly that the decision concerning just how many and what Boards for the Certification of Specialists should be allowed, rightly came under the authority of the American Medical Association, *(via* action of its Councils on Medical Education and Hospitals) and they could not conceive that such important functions should be usurped by a National Board not an integral part of the executive machinery of the Association and having in its personnel many men not engaged in practice—indeed, several men who were not even active members of the Association. Therefore, the Committee, scorning to "play politics", sought redress through the Association's constitutionally available channels.

Openly, at a general session of the House of Delegates, appeal was made by both the Gastro-Enterological and the Proctological Committees for recognition and for authority to inaugurate, incorporate and put into operation, Boards for the certification in their respective specialties. The Speaker of the House referred the motion to the Councils on Medical Education and Hospitals. These Councils willingly granted a hearing to the petitioning Committees and courteously listened to the arguments presented. No member of the National Board appeared before the Councils to challenge the arguments, to show cause why the organizations sought should not be allowed and supported or to explain why the National Board had acted in so abrupt and unorthodox a fashion at the "eleventh hour" and contrary to the attitude which, for more than a year, had been maintained by the National Board towards gastro-enterologists and proctologists.

After mature deliberation, the Councils recommended to the House of Delegates that in their judgment, the petitions of the two groups of specialists in practice (gastro-enterologists and proctologists) should be granted. From the viewpoints of fairness, usefulness in the proper regulation of specialism, in practice and of consistency, it would seem that no other course was open to the Councils. As one conscientious and broad-visioned Member of the Councils stated, "work in this field (gastro-enterology) has been recognized long ago by the establishment of a Section (in the American Medical Association's annual proceedings) and since encouragement to the development of this Board (for the Certification of Gastro-Enterologists) had been given, a measure of obligation (to recognize the Gastro-Enterological Board and permit its incorporation and functioning) was involved".*

Naturally, the actions of the Councils on Medical Education and Hospitals and of the House of Delegates of The American Medical Association are gratifying to the Committee responsible for the establishment of a National Board for the Certification of men trained and competent to serve the public, the medical schools and hospitals. Just as is the case with regard to those who devote their energies to such special fields as cardiology, pulmonary affections, allergy, syphilology, dietetics and nutrition, mature-visioned and experienced men readily recognize that the adequate practice of gastro-enterology calls for more than can be expected of the general internist. The specialty requires not only a thorough grounding in internal medicine but in addition demands an appreciation and understanding of modern experimental physiology, organic chemistry, parasitology, roentgenology, pathology, nutrition and dietetics. It is this special experience superimposed upon the training necessary to qualify as a reliable internist which, when acquired, means that its possessor truthfully can be classed as a gastro-enterologist. The securing of this special knowledge usually indicates that the internist has devoted much time to post-graduate study, to travel, attendance at the meetings of special societies and has invested considerable capital in books, magazines, apparatus and equipment wholly foreign to and not demanded of one who chooses to continue as a general internist. Usually, the gastro-enterologist contributes considerable time and effort to the dispensary and clinic—some of which labor is not entirely agreeable, esthetically considered.

For example: Not infrequently, even though his work may be considered lightly in certain quarters where what constitutes a gastro-enterologist is so little understood or appreciated that the specialty is spoken of slightingly or is unrecognized, a hospital's dietetic efficiency and down-to-dateness—nay, even its very equipment—are made the responsibility of the gastro-enterologist. One need but inspect the diet kitchens of any hospital in order to learn whether or no the specialty of gastro-enterology is recognized in that institution. When it is *not*, "dieting" means not the exhibition of foods most conducive to aiding the individual patient and to combating his affection. In such a hospital, unless the services of a dietitian trained elsewhere by a gastro-enterologist or an expert in nutrition have been hired, one finds that "dietetics" means only a miscellaneous collection of typed sheets: "Spilly's Ulcer Diet", "P— Hospital's 6,000 Calorie Diet", "Chronic Ulcerative Colitis Diet", "Schmidt's Test Diet", "Acute Nephritis Regime", "Anti-fat Routine", "Anti-Ketogenic, No. I and No. II", "Pemberton's Diet for Rheumatism", "Diet for Diabetes", "Weir Mitchell Treatment", "Minot's Liver Diet" —and so on *ad infinitum*. The list becomes augmented on the publication of each new text-book on "Diet and Nutrition" or whenever a "Big Chief" returns from a medical meeting where, usually from the thesis of a real gastro-enterologist or one conversant with advances in nutrition, he has gleaned "something new".

Sad though it may be to admit, "dietetics" of the above sort in the majority of our hospitals is the rule and not the exception. And we are referring not to hospitals located in such communities as Pelican Rapids; Cadiz, Missouri; Bedford,

*Clauses in parentheses inserted by the Editor to insure clarity; otherwise the quotation is literal.

Vermont; many so-called "metropolitan" hospitals or institutions styled "medical centers" serve no more efficiently. Too often, the patient is fitted to the diet and the diet is not ordered and exhibited for the peculiar (often varying day by day) needs of the individual.

Evidence is available that "internists" allied to those who are responsible for the above cited example of dietetic inefficiency in many hospitals also are the sources from which have sprung opposition to gastro-enterology's being recognized as a specialty in medicine. While no really trained, busy or broadminded internists object to certain of their colleagues limiting their work to diseases of digestion and nutrition—in fact, welcome such specialization and when they are ill of these affections consult the gastro-enterologist rather than the general internist—yet, it has been observed that there is a type of internist's mind which possesses such a degree of self-satisfaction that it does not hesitate to attempt the diagnosis and treatment of all affections which lie in the broad field of medicine. These unfortunate fellows don't know that they don't know: hence, their assertiveness. It is the patient who suffers most from their spreading thinly over a large area a degree of knowledge which, were it concentrated in one field, might permit reasonable competence. However, the idea of limiting one's efforts to a particular group of ailments cannot be conceived by these "inclusive internists": they themselves, are "specialists in everything"! Hence, they are militantly, often vocally and abusively, intolerant of that internist who chooses to confine his endeavors to cardiology, tuberculosis, the anemias, renal affections, diabetes or diseases of the digestive tract: particularly are they antagonistic to the last named. Just why, it is difficult to say, for indeed, with some internists, antagonism to the gastro-enterologist amounts almost to an obsession.

All of this opposition does not seem to be the mere defense of the principle that any really *trained* medical man should be as competent to engage in practice in the above-named divisions of medicine as are those internists who have given much time and effort to the acquirement of special knowledge. It would seem that much of the vocalized "principle of the thing" is in great part professional smugness or even selfishness: there is reluctance to admit certain limitations in experience; there is intense disinclination to having the great group of digestive ailments and disorders of nutrition dominating all medical services, pass to one equally competent as an internist but who has had ambition and has secured added training in gastro-enterology. The professional "dog-in-the-manger" will not inconvenience or burden himself by the effort needed to acquire intensive and specialized experience and yet he won't allow to work, unscathed, those who have toiled and are more capable.

That this attitude exists and actually is the main source of opposition to gastro-enterology's becoming recognized as a specialty in internal medicine and a Board of Examination and Certification's being approved, plainly was shown by the recent bitter debate which developed when the New York Academy of Medicine ruled against the setting up of a local section in gastro-enterology. That hearing brought out not only the professional selfishness of the opposition but what was most discouraging, professionally and scientifically, that those internists most positive, one might say, pugnacious, in their disapproval of the establishment of the proposed section, were men who have contributed nothing to research, pathology, diagnosis or treatment in alimentary tract ailments. Nevertheless, daily in lectures, clinical work and private practice, they employ tests, special methods and information painstakingly accumulated and generously passed on to them by the very gastro-enterologists who sought recognition, who were refused it and whom they damn. To a trained internist, they insist, "There are no specialistic demands in gastro-enterologic practice!" When thus they babble they classify themselves with that notoriously smug laboratory worker, who refused to grant any greatness to the beloved Osler, stating that "any ordinary capable physician could learn the diagnostic medicine, which Osler knew, in six months!"

New York is not unique in such opposition to gastro-enterologists and the wholesale appropriation and pirating of the results of their labors: many large medical centers throughout this country can qualify quite as completely.

The crystallization of the above-mentioned "back-stage" influences for opposition to a special Board of Gastro-Enterology occurred at the 1934 Cleveland Session. Strong personal and institutional pressure was brought to bear upon certain "key" members of the National Board so that by intra-Board politics, secret sessions and intense personal activity, these "key" members so were able to influence their fellow-members and to group the specialties which they "approved" that gastro-enterology was not included. That there were displayed "eleventh hour" tactics of a type to which right-minded men of our profession would not stoop, whatever might be the prize, was most obvious. With little fear of contradiction, one may state that gastro-enterology's most articulate, persistent and politically efficient critic and enemy was a National Board Member who never practiced medicine, never contributed anything to its scientific advancement, always has held purely "pen and ink" jobs in our profession, is well known as a marvelously expert, ear-to-the-ground type of medical-institution executive, and who, nevertheless, had the effrontery to conduct a campaign against a section of the Scientific Assembly of the Association and its research and clinical supporters! That this member of the National Board within a month after the 1934 Cleveland Meeting, was the recipient of an "executive plum",

carrying a heart-warming salary, in the institution where had arisen the most virulent, New York opposition to the gastro-enterologist, would appear to prove that he was working not wholly without ulterior objectives. To the "principle" about whose upholding this member waxed so eloquent at Cleveland, the medical Tammany which employed him added very satisfactory "interest" when he "brought home the bacon". If his efforts had not so prospered, doubtless the jobs which already he held would have been on the auction block!

However, the ideals for which representative internists, who choose to be gastro-enterologists, labor, have not been abandoned. Along proper, decent and ethical lines, the Committee will proceed and will seek to establish and to have recognized a Board whose stamp on a physician will mean that he is dependably trained in an exacting and needed specialty. Ultimate success is assured. Those opposing the efforts are but postponing the day when our profession and the public better will be served. Such delay need not be. Groups responsible for it do not deserve to be classed as progressive, altruistic, broad-gauged physicians. The lay public has a right to know that there is a vast difference between a gastro-enterologist and a "stomach specialist". In how many communities do mediocre men, of no special training and experience, practice as self-designated "stomach specialists" because no Board or authority exists which may regulate modes of practice often not far removed from quackery? How often do the inefficiency and tinkering of these doctors nullify our expensive, nation-wide, anti-cancer campaigns? Internists who have devoted years to obtaining experience and facility in the diagnosis and treatment of patients affected with digestive disorders are entitled to just as much professional and lay recognition as are surgeons who devote their energies to ailments of the eye, the ear, the bony skeleton, the central nervous system.

The American Medical Association is the parent organization to all practitioners. It has seen fit to grant gastro-enterology (and proctology) the dignity and responsibility of a section of its annual Scientific Assembly. Through its qualified Councils, the Association should have the final decision as to what groups be acknowledged sufficiently important to set up Boards for the regulation of special practice. Decisions so weighty should not be dictated to the Association by a self-perpetuating National Board whose actual relationship to the American Medical Association is but an advisory one: a Board, a large proportion of whose members have not met, and in certain instances never will meet, the exigencies and demands of medical practice: a Board which the most vocal, biased and politically-minded member attempts to dominate and who seeks to deprive of rights Fellows of the Association, rights earned by long support of the parent organization, by education, training, scientific research and clinical experience.

Our institutions for medical teaching, our hospitals and our citizens lamentably are lacking in that knowledge and service which only qualified gastro-enterologists are capable of providing. Progress towards a better appreciation of the physiology of the organs concerned with digestion, absorption, elimination and nutrition depends upon the gastro-enterologist. Through him the researches of the physiologist, the chemist and the pathologist are supported and their discoveries translated into clinical procedures which permit greater accuracy in diagnosis and more dependable treatment. The literature of the past thirty years demonstrates how richly gastro-enterologists have contributed to science and practice: scarcely a fundamental advance in diseases of digestion and in nutrition has been made by internists other than those who have been concerned with some phase of gastro-enterology.

How rapid and how significant may scientific gastro-enterology progress in the future, to a large degree, depends upon what standards for practice are set for those who work in that specialty. In our own hands lies the decision. Support of the program initiated by the Committee delegated to form a Board of Gastro-Enterology gives assurance of better teaching and more enlightened practice. Only unreasonable bias and petty professional politics have prevented unanimous and whole-hearted backing of the Committee's plans. Those plans are summarized by the data printed below.

The adoption of the formulae suggested means that the day will be hastened when, on a foundation definitely more solid than personal urge or desire, may a physician dub himself as a "stomach specialist". The Committee's plans, when consummated, will assure our profession and the public that every person sanctioned by the Board of Gastro-Enterology is, first, a thoroughly competent internist and, second, he has had training and experience which certify that, to a degree greater than possible by the general internist, he is qualified to investigate, diagnose and treat diseases of digestion and nutrition.

Frank Smithies, Chicago.

PROPOSED CONSTITUTION AND BY-LAWS OF THE AMERICAN BOARD OF GASTRO-ENTEROLOGY

Article I.

Name.

The name of this corporation shall be the American Board of Gastro-Enterology. (Gastro-enterology is defined in accordance with the Articles of Incorporation as "the branch of medical practice which deals with diseases of the digestive system and nutrition".)

Article II.

Purposes.

The purposes of the Board are as follows:

(1) To encourage the study, improve the teaching and elevate the standards of gastro-enterology.

(2) To conduct examinations and issue certificates to licensed medical practitioners who shall qualify as competent to practice gastro-enterology.

(3) To serve the public, physicians, hospitals and medical schools by preparing lists of specialists and practitioners who have been certified by the Board.

Article III.

Membership.

Section 1. *Qualifications of Members.* Each member of this Board shall be a physician, duly licensed by law to practice medicine, and each shall be a member of the constituent society which has nominated him for membership on the Board.

Section 2. *Number of Members and Duration of Membership.* The membership of this Board shall consist of four members from each of the nominating societies, viz.: The American Gastro-Enterological Association and the Section on Gastro-Enterology and Proctology of the American Medical Association, each member to be elected for a period of four years, or until his successor shall have been appointed. The eight original members at the time of incorporation, in 1934, shall be divided into four classes, whose terms shall expire in 1936, 1937, 1938 and 1939 after the annual meeting and thereafter a new member shall be elected every year by each parent organization, to fill the vacancies.

Section 3. *Time and Manner of Admission to Membership.* A member designated by a nominating society shall take office at the expiration of the term of the member whom he is designated to succeed, except that a vacancy or vacancies may be filled for the unexpired term in the manner provided in these By-Laws. A member appointed by one of the nominating societies shall be furnished with evidence of his appointment and shall become a member of the Board upon presentation of such evidence at any legal meeting of the Board.

Section 4. *Change in Number of Members.* The number of members from each of the nominating societies may be increased or diminished by recommendation of the Board and approval by both nominating societies.

Section 5. *Designation of Additional Nominating Societies.* Nominating societies in addition to those named in the Articles of Incorporation may be designated upon recommendation of the Board and approval by the then existing nominating societies.

Section 6. *Vacancies in Membership.* Any vacancy created in the membership of the Board by resignation, death or otherwise, before the expiration of term shall be filled by a member of the nominating society from which the member was nominated whose resignation, death or other incapacity created such vacancy. Appointment to such vacancy shall be made for the unexpired term by the President of the nominating society or in such other way as each nominating society may determine.

Article IV.

Meetings.

Section 1. There shall be an annual meeting of the Board in each calendar year, the time and place to be fixed by vote of the Board.

Section 2. Special meetings may be called by the President of the Board or upon the written request to the Secretary-General of three members of the Board. Written notice of special meetings shall be sent to each member of the Board not less than twenty (20) days prior to such meeting, with a statement of the purpose of that meeting.

Article V.

Quorum.

A majority of the members of the Board shall constitute a quorum for the transaction of business.

Article VI.

Officers.

Section 1. The officers of the Board shall consist of a President, a Vice-President, a Secretary-General, a Treasurer, a Board of Regents and such other officers as the Board, from time to time, may designate.

Section 2. Each of the officers of the Board shall be elected at the annual meeting by majority vote and shall hold office for one year or until his successor shall have been elected.

Section 3. *Vacancies.* A vacancy in any office may be filled for the unexpired term by election at a special meeting of the Board called for that purpose or by mail ballot of the members of the Board.

Section 4. *Duties of Officers.*

(a) *The President* shall have the powers and duties usually appertaining to such office. He shall submit to the annual meeting of the Board a written report of the Board's business, activities and affairs.

(b) *The Vice-President,* in the absence or disability of the President or at the latter's direction, shall perform all of the duties of the President.

(c) *The Secretary-General* shall keep in proper form minutes and records of all corporate proceedings, meetings of the Board and all data with regard to examinations, the issuance of Certificates and other transactions of the Board. He shall be the Custodian of the corporation's seal and shall affix the same when and wherever proper.

(d) *The Treasurer* shall keep, or cause to be kept, true and accurate accounts of all financial

transactions of the Board. He shall be the Custodian of the funds of the Board and of any securities which are the property of the Board. He shall prepare or cause to be prepared an audit of the corporation's books and shall present a report of such audit at each annual meeting of the Board. The Treasurer may be required to give bond in such sum as may be determined from time to time by the Board.

(e) *The Board of Regents* shall consist of the officers of the corporation and four other members, and shall manage the business of the corporation. Three members shall constitute a quorum for the transaction of business.

(f) *Subordinate Officers* may be appointed by the Board from time to time in such number and with such powers and duties as the Board may decide.

Article VII.

Applicants for Certificates.

Section 1. *Method of Making Application.* Application for Certificates shall be made to the Secretary-General upon a prescribed form. Each application shall be accompanied by a fee in such sum as the Board, from time to time, may fix, and shall also be accompanied by an unmounted, autographed, recent, and dated photograph of the applicant.

Section 2. *Requirements for Applicants.* Each applicant must establish in a manner satisfactory to the Board:

(a) That he is of high moral, ethical and professional standing;

(b) That he is a graduate of a medical school which is satisfactory to the Council on Medical Education and Hospitals of American Medical Association;

(c) That he is a physician duly authorized by law to practice medicine;

(d) That he is a member of the American Medical Association if resident in the United States or by courtesy, a member of such Canadian Medical Societies as are approved by the Council on Medical Education and Hospitals of American Medical Association;

(e) That he has completed an interneship of not less than one year in a hospital approved by the same Council;

(f) That he is a qualified internist:

(g) That he has had sufficient and satisfactory training and experience in the practice of gastro-enterology.

Section 3. *Classification of Applicants.* Applicants for recognition by the Board shall be divided into two classes, according to length of practice:

A. Fifteen years or more of practice limited to or principally devoted to diseases of digestive system and nutrition.

B. At least seven, but less than fifteen, years since graduation from medical school.

Section 4. *Examination of Applicants* of each class:

Class A. Applicants who have qualified under Class A shall be required to undergo and pass satisfactorily a practical, oral and bedside, clinical and laboratory examination, including interpretation of roentgenograms. The Board, in view of applicant's training, published records and professional work in his community, may use its discretion as to the extent of the examination.

Class B. Applicants who shall have qualified under Class B, shall be required to present evidence of

1. A period of study, after the interneship, of not less than three calendar years in clinics, dispensaries, hospitals or laboratories recognized by the Council on Medical Education and Hospitals of the American Medical Association as competent to provide a satisfactory training in gastro-enterology.

2. This period of specialized training shall include

(a) Intensive graduate training in the anatomy, physiology, biochemistry and pathology of the alimentary canal and its appendages and special training in roentgenology;

(b) An active experience of not less than eighteen months in hospitals, clinics, dispensaries or diagnostic laboratories recognized as competent in gastro-enterological work;

(c) Examinations in the subjects mentioned under (a) as well as written, oral and practical examinations in the clinical, laboratory and public health aspects of gastro-enterology.

3. An additional period of not less than two years of practice.

Article VIII.

Certificates.

Section 1. Certificates to be issued by the Board shall be in such form as to comply with the Articles of Incorporation, shall be signed by the President and the Secretary-General of the Board and shall have placed upon them the Official Seal of the Corporation.

Section 2. Certificates shall be issued only after approval by three-fourths of the members present at any legal meeting of the Board.

Section 3. *Revocation of Certificates.* Any Certificate issued by the Board shall be subject to revocation in any of the following events:

(a) That the issuance of such Certificate or its receipt by the physician so certified shall have been contrary to or in violation of any provision of the Articles of Incorporation or of these By-Laws;

(b) That the physician so certified shall not have been eligible in fact to receive such certificate;

(c) That the physician so certified shall have made any misstatement of facts in his application or in any other communication to the Board or its representatives;

(d) That the physician so certified shall have had his license to practice medicine revoked or

shall have been expelled from one of the nominating societies which name the members of this Board.

Section 4. *Rules and Regulations.* The Board may adopt such further rules and regulations governing examinations and issuance of Certificates as the Board may from time to time decide.

Article IX.

Amendments.

Amendments to these By-Laws may be made by a majority vote at any of the Board meetings, written notice to each member having been given of such intention twenty days (20) in advance of the meeting.

Article X.

Seal.

The Seal of the Board shall bear the following: "The American Board of Gastro-Enterology, incorporated in the State of Delaware, 1934", or words and figures of similar import.

The Committee Appointed by the American Gastro-enterological Association, The Section of Gastro-enterology (and Proctology), The American Medical Association.

TYPOGRAPHICAL CHANGES

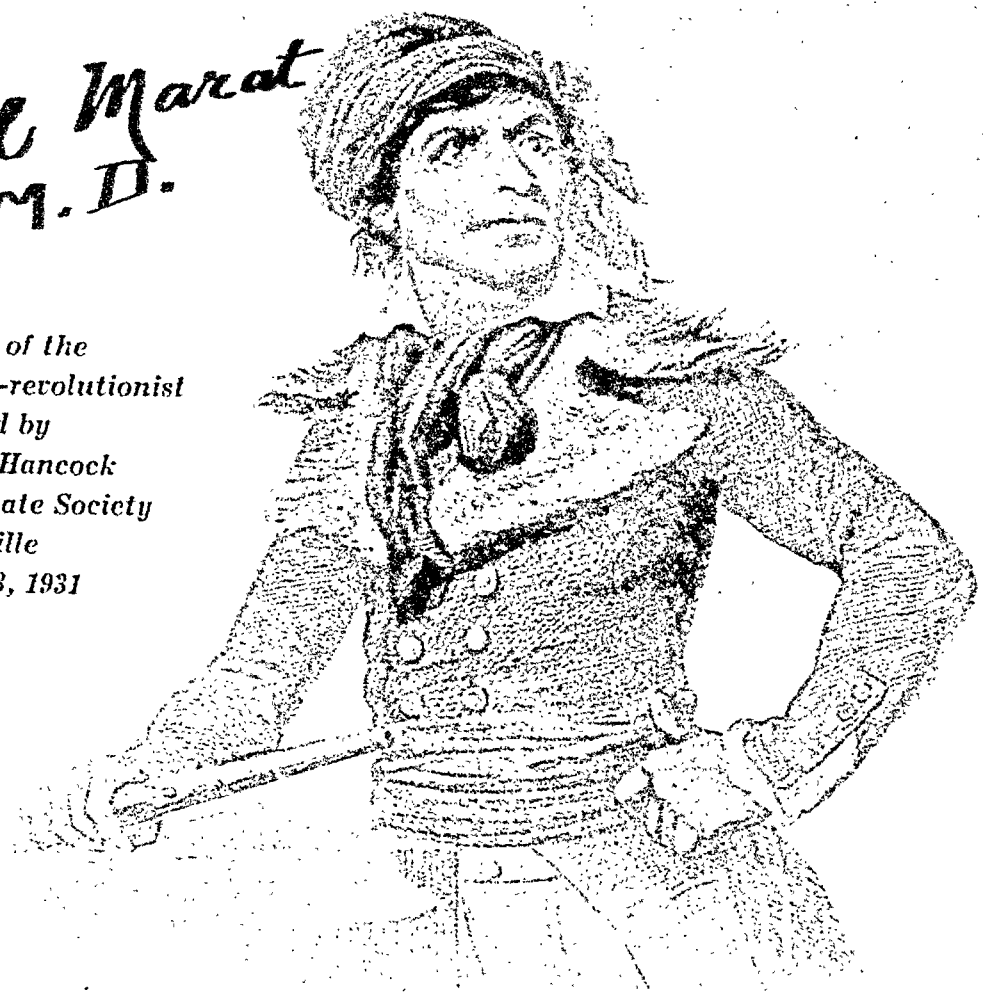
The response to our editorial in the October issue was quite lively. Many letters were received indicating that the matter of a better typographical format is one that physicians take seriously. The tendency, judging from these letters, is toward the feeling that medical journals always have hung back in this matter but that there is really no good reason forever to disregard excellency in printing.

Armed with this opinion, we have in the present number gone as far toward modern arrangements as we believe is desirable or necessary. The special treatment of the After "Hours" section emphasizes the essential difference between the cultural topic and the more strictly clinical and scientific. A narrower column width, the slight, almost unnoticeable separation of the printed lines by means of a wider slug, a few alterations in headings, the employment of "rules" to separate articles, and greater study and planning of the placement of illustrations are improvements which will give increased reading ease to our subscribers, and yet in no way appear sensational. It is to be hoped that the work of the Supervising Editor will continue to be facilitated by the helpful and constructive suggestions of readers, whose advice already has proved invaluable.

Beaumont S. Cornell.

Jean Paul Marat M. D.

This story of the
French Physician-revolutionist
was read by
Dr. J. Duffy Hancock
at the Innominate Society
Louisville
October 13, 1931



Marat, the Champion of Liberty, the Leader of the Revolutionists

RECENTLY, chance references in reading called to my attention a curious similarity between two outstanding men of the 18th century. Although separated nearly a hundred years in time and three thousand miles in distance they had many traits in common. Both possessed unusual intellectual ability and attainments, both acquired medical degrees, both found other spheres more attractive than science, and both are remembered, justly or unjustly, for their association with movements resulting in the destruction rather than the preservation of life.

One was John Cotton Mather, graduate of Harvard University in the three schools: law, theology, and medicine. His life and his connection, guilty or innocent, with the Salem witchcraft trails might be as interesting a study as the subject of this essay, Marat, one of the leaders of the French Revolution.

EARLY PART OF THE FRENCH REVOLUTION

Even if this entire paper were devoted to a resumé of that important movement it would be quite inadequate. However, a few of the outstanding events must be mentioned in order to give a proper background to the presentation of this most interesting character.

Extravagance, oppression and indifference comprised a triple yoke under which most of the French people had labored for many years. At about the middle of the 18th century the first rumblings were beginning to be heard. The Encyclopaedists under Diderot and the Economists or Physiocrates, writing mostly from healthier residences in other countries, called attention to the numerous injustices and cried for reforms. Their influence, however, was not extensive since hard thinking was required of their followers. At about the same time Rousseau making similar appeals but advocating more radical measures and playing more upon the emotions of the common people, became a leader easy for the mob to follow. The constant demand for money for the court had entirely exhausted the lower classes and in 1789, Calome ordered a tax upon the nobles. This shocking and irritating procedure led them, in 1789, to call an assembly of the States-Gen-



MARAT'S MURDERESS, CHARLOTTE CORDAY, painted from Life by Jean-Jacques Haver in the prison of the Conciergerie.

eral which had not met since 1610. This body was composed of three divisions, the nobles, the clergy and the third estate, or commons. When the body met the first matter of importance was the distribution of voting strength. Voting as units, the nobles and clergy, representing but 1/25 of the population, could control all legislation. The representatives of the third estate naturally insisted upon individual voting by the various delegates and not by divisions. Because of their insistence they were excluded from the Palace at Versailles, the meeting place of the States-General. They then withdrew to an abandoned building which had once housed a tennis court and there took the famous "Oath of the Tennis Court" agreeing never to disperse until they had made a new constitution for France—and in the next breath shouting "Long live the King", showing their greivances were against the government rather than the person of the king. The National Assembly thus formed established National Guard Units in many of the larger cities. On July 14, 1789, less than a month later, the Bastille was destroyed—not especially to free prisoners but to show how the mob felt regarding what it stood for. The people were thoroughly aroused but their feeling was little understood or much belittled, as the only notation made by Louis XVI in his diary for that day was the single word "Nothing". The frenzy of the people born of the natural causes of want and hunger was nourished by radical publications and speeches of the leaders of that movement rapidly developing into the French Revolution. In these efforts no greater influence was exerted than that wielded by Jean Paul Marat, "Darling of the Scum of Paris", and publisher of "The Friend of the People." While he could not be called a dual personality since he did not alternate his activities throughout his life, he might have been said to have lived two lives—one, that of a scientist, ending in 1789, or a little earlier, and the other, that of a revolutionist, beginning at that time and terminating at his death four years later. As we are primarily interested in his scientific life, so generally unappreciated, we shall first consider it somewhat in detail and in closing continue our sketchy review of the revolution and the part he played.

BIRTH AND PARENTAGE

Jean Paul Marat was born in 1743 at Beaudry (or Boudry) in the province of Neuchatel, Switzerland, the province at that time, however, being a Prussian possession. His parents were respectable people of the lower middle class. The family name was originally spelled M-A-R-A but Marat added the "T" when he went to Paris in order to make it appear more like a French name. His father was a teacher of languages and a designer of figures of cloth. He was a native of Sardinia and had originally been a Catholic, but on coming to Switzerland had accepted Calvinism. The belief that there was a possible Semitic strain is based upon these facts: first, in the classic times many Carthaginians came from Africa to Sardiana; secondly, the word "marah" (M-A-R-A-H) in Hebrew means "bitterness", which was destined to be a most appropriate name for the figure of this essay, and thirdly, that the marriage registry record notes that the father's witness was a Jew, Paul Abraham Medez. The mother was a Swiss, Louise Cabrol, and her father a Frenchman. It seems that Marat was fortunate in having the



Marat the Physician, Scientist, and Statesman. Born 1743; Murdered 1793.

heritage which he did in those times. His father instilled in him a love for learning and to his mother he owned his spiritual life dominated by justice, philanthropy and a love of glory. Most of his inconsistencies in later life are probably attributable to that last trait, the love of glory.

Marat was the first-born of several children. There are records of three other children and references to two more. In particular contrast to Marat's life was that of his brother David. Marat found the Revolution an opportunity to work for France; David found it an excuse to leave. Before the excitement was too intense he went to Russia where Catherine the Great permitted him to change his name to M. de Bouderic. He taught French at Tsarke-Salo and led a quiet studious life. After he left France he and Marat did not correspond. He lived to be a hundred years of age but had no other distinctions—certainly in all those hundred years he did not even taste the experiences of real life which were so crowded into Marat's eventful four big years, 1789 to 1793. Albertina, a sister, lived for years in poverty with Marat's widow and worked with her in the publication of his biography and the effort to clear his name of the infamy heaped upon it by his enemies several years after his death. A second brother, Oliver, was also not present during Marat's revolutionary activities. He was busy at that time collecting and mounting insects at Geneva. Shortly before Marat's death the government had confiscated a valuable collection of minerals which it had stored at the Jardins des Plantes. There were no funds available for the care of this collection and it seemed destined to be lost. Marat's popularity, immediately after his death, was capitalized to secure funds for salary and improvement of living quarters at the museum for Oliver, who was appointed director of the institution. In this way the collection was saved. After Robespierre's death Oliver was forgotten and disappeared. No information was procurable concerning the other two children; according to some biographers there were no others. So much for the family.

EARLY EDUCATION

Of his, Jean Paul's, early education we know little except that certainly it was above the average. He could speak fluently in French, Dutch, Italian, English and Spanish. At the age of 16, he solicited of Louis XV the favor of being attached to a Royal Expedition on its way to Tabolsk to watch the passage of Venus over the sun. Because of his youth his request was denied. The following year, however, he left home, accompanying some wealthy tourists to Bordeaux where he served as tutor in that prominent family. He continued his own studies in the university there at Bordeaux, and later at Toulouse and at Paris, taking courses in politics, philosophy, literature and medicine, and devoting much time to optics and electricity. His education was further rounded out by shorter periods of study at Amsterdam, The Hague and Utrecht.

FIRST RESIDENCE IN PARIS

In 1762 he located in Paris and shortly afterwards began to practice medicine. He was not a prolific writer then for we have found reference to only one publication, a pamphlet entitled "A Remarkable Disease of the Eye, Cured by Electricity, Which Had Been Considered Incurable". While he seems to have established a fairly successful practice, he did not achieve anything like

the reputation he did in London where he went in 1765 at the age of 22.

RESIDENCE IN THE BRITISH ISLES

His first years in the British Isles were spent in study, at least part time. He resided in London, Dublin, and Edinburgh and while there is no record of university attendance at any of those places he probably did attend lectures there and in other schools since the title pages of most of his publications mention his being a graduate of several English Faculties. Of one degree, we are certain. It was an M.D. given on June 30, 1775, by the University of St. Andrew's in Scotland. This was also the school attended by Dr. Oliver Goldsmith. While the degree was in a sense an honorary one conferred upon the recommendation of two outstanding physicians, certainly it was not so ephemeral as the one awarded or supposed to have been awarded to Goldsmith. At that time Marat was a real student possessing both the desire and industry to increase and apply his education. Between 1770 and 1773 he was at various times at Newcastle where he aided in combating an epidemic. His work there evidently was satisfactory as he was given a diploma conferring upon him the freedom of the city.

His first publication in English, presented in 1773, appeared originally as a "Treatise on the Soul", but was expanded into a "Philosophical Essay on Man, being an attempt to Investigate the Principles and Laws of the Reciprocal Influence of the Soul and Body". In this essay he tried to show the importance of science to a proper understanding and explanation of philosophy, maintaining that philosophy could not solve all problems unaided as most thinkers then held. For this opinion he was ridiculed by Voltaire and thus an enmity of long standing was engendered. At another time when he wrote that "thought could make a man enjoy nothingness" he was again enraged at Voltaire who sarcastically answered, "It (nothingness) is a great empire; reign there, but insult a little less those who are something". It is not difficult to understand the reaction such a reply would cause in Marat or any one of us. Returning to his "Essay on Man" we find that the term "soul" is not used here in the spiritual sense but in the sense of consciousness in general. In this essay, which shows Cartesian influence, he advances the theory that the body and soul are two distinct entities with no direct relationship between them. However, a certain agent, his "nervous fluid", brings the soul and body into relation, one with the other. That fluid, which is the vitalizing power of the nervous system, gives physical qualities and elasticity to soul (consciousness) in the meninges, basing this upon the following reasons: first, the slightest inflammation of the meninges affects the mind; secondly, it is possible to mutilate the brain itself without affecting the mind, and thirdly, that ligation of a nerve is followed by abolition of sensation below the ligature. This last observation was the result of personal experimentation which led him to the conclusion that impressions did not reach the soul since the flow of nervous fluid was interrupted. Many other interesting opinions are offered in this essay. Pity is described as an artificial sentiment acquired by association and generated in the heart only by prudent reflection. Marat observed that love accelerates the pulse, brightens the eye, animates the expression and gives life to our tasks and grace to all our movements. He attempted to add to the special senses the two additional ones of hunger and thirst. The sense of touch was not regarded as being limited to the skin but as being active also in the interior of the body; confirming this view by recalling the impression of the sweetest kiss or the painful misery of an acute colic. Another opinion expressed was that all men are controlled by the constitution of their bodies and the character of their minds; the difference in minds being due to the disposition of the various organs. The essay is quite lengthy; many other selections from it might be offered. While it is critical of everyone and is considered by many as rather immature, it was original in manner of presentation and showed unusual familiarity with the works of Galen, Aristotle, Plato, Socrates, Montaigne and Descartes in questioning their mental capacities and exposing their errors.

In the following year, 1774, he wrote the "Chains of Slavery", his first political publication. Marat was an ardent admirer of the English freedom of government, or rather of its possibilities if properly followed. This paper was not particularly radical, being somewhat like a letter a public spirited physician of today might write for the open letter column of one of our daily newspapers. In it he demonstrated the non-representative character of Parliament, exposed the falsehoods and diplomacy of the upper classes and urged the election of sincere representatives. Lord North, the Prime Minister, had the article suppressed. It was, however, published subsequently in Holland and secretly distributed in England, but too late to affect the election. That the paper struck a popular chord is evidenced by the fact that Marat was given the freedom of several cities in the northern part of England and admitted shortly afterwards to the Masonic Order. In his reaction to the suppression of this article, which was little more than ordinary or perhaps ill-advised censorship, one first observes the bitterness and fury with which opposition filled him. He regarded it as persecution, cruel in that it checked the accomplishment of something which he honestly believed was for the good of the people.

In June of the next year, 1775, Marat published his first strictly medical paper in English. It was an "Essay on Gleet" and was dedicated to the

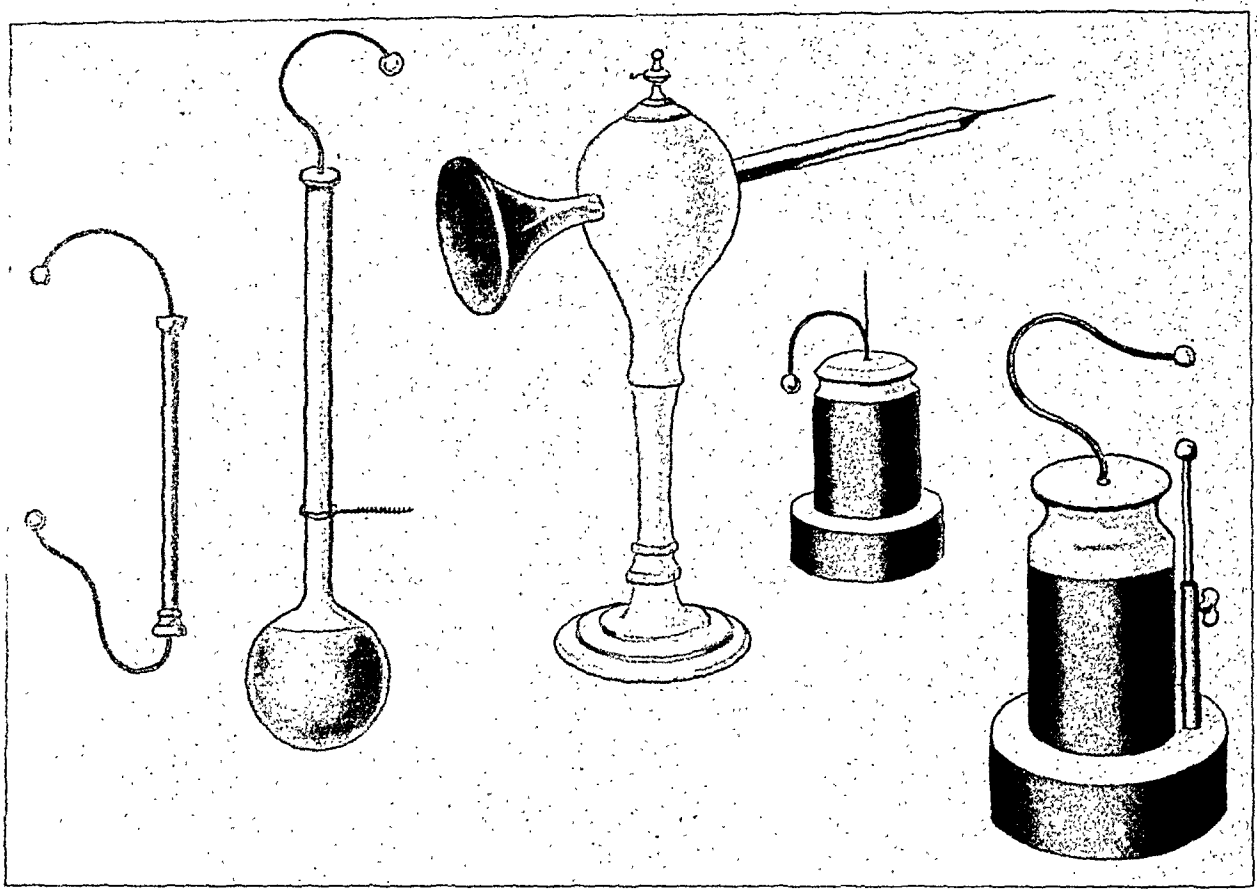
Worshipful Company of Surgeons in London. This paper is rather modern in tone and shows scientific approach to the subject. Using pathological dissection he demonstrated for the first time the underlying condition which we now recognize as one of the important causes of chronic urethritis, i. e., that the infection, universal in the acute case, extends in the chronic case into muscular layers, the glandular structures and the *lacunae*. His treatment consisted in first probing for the sensitive points and then inserting a soft wax bougie which had been anointed at corresponding points with some "suppurative" rather than the usual desiccative plaster, generally using diachylum. The plasters were retained for various lengths of time by bending the outer extremity of the bougie. When the plasters were removed Marat advised *irrigation* of the urethra with *sal ammoniac* diluted in water in order to flush the follicles of suppurative debris. The bougie was then replaced. As improvement occurred milder plasters were used. Throughout the course of treatment careful attention was given to the patient's general condition: this was an unusual departure in those days. Marat also had a good knowledge of strictures, defining them accurately and diagnosing them by symptoms.

In spite of his competence in this line of work, (he does not hesitate to praise himself and deride his competitors), he is somewhat apologetic for doing this class of practice and makes it clear that it was only a side line, as do so many today.

His other important medical contribution in England was an address a year later, 1776, to the Royal Society on "An Enquiry into the Nature, Cause and Cure of a Singular Disease of the Eye". The disease in question was *gutta serena,* classified also as "accidental presbyopia", which was characterized by congestion and consequent swelling of the muscles of the eyeball with subsequent pain, stiffness, irregular action, weakened sight and lack of accommodation. The usual treatment was to induce vomiting by purging, salivation and ammonia fumigations. Marat believed the disease due to non-assimilation of mercury salts (a commonly used drug, then as now) with absorption of the mercury particles in the arterial and venous coats of the eyeball. He, therefore, contradicted the usual treatment and prescribed relaxation of the nervous system, rest, quiet, low diet, no strong drinks (using only barley water, whey, and marshmallow infusion), moderate bleeding at the foot once a week, and other measures to reduce ocular ten-



Marat, triumphant, when the Firebrand of the French populace.



Electrical instruments made by Marat, from an illustration of his work, "Researches on Electricity."

sion, e. g., local emollient poultices (such as oatmeal) and quassia for clarifying the humors and diluting the body fluids. Occasionally he used electrization and observed that it was much more effective if congestion were previously reduced by bleeding. In order to observe the progress of a case Marat improvised a comparative eye scale, determining in inches how near the hands of a watch could be seen.

Marat left London for Paris in 1777. His stay in the British Isles from 1765 must have been a pleasant one. At his office in Soho Square he had a fashionable practice. He associated with the *elite* of the scientific, artistic, and literary worlds. He was a patron of the London coffee houses where there were often interesting gatherings and conversation. At one such meeting, he met Benjamin Franklin, who had a kind interest in him from then on, championing his cause in his work on electricity later in Paris.

Before following him to Paris let us consider the "criminal charges" which some historians have made concerning him during the years just reviewed. That he was said to have been convicted of theft and imprisoned for debt during this time may be due to the confusion of his name with that of the international crook, John Peter le Maitre, alias Maire, and alias Mara. It was more likely due to a deliberate attempt by his enemies to discredit him. It seems proper to accept the answer made by Marat himself. In 1790, he said, "Since the age of 16, I have been absolute master of my conduct. I have lived two years at Bordeaux, ten in London, one in Dublin, one at The Hague, Utrecht and Amsterdam and nineteen years in Paris. I have traveled over the half of Europe where one is compelled to register with the authorities. I defy anyone to find my name noted for any unlawful act. Moreover, I defy any person under the heavens to reproach me with a dishonest act".

SCIENTIFIC LIFE AFTER RETURN TO PARIS

Why Marat returned to Paris in 1777 largely is a matter of conjecture. There was no woman involved in the case, and he had a successful practice, and many congenial and elevating associates. It may have been that he became homesick for life on the continent, he may have wanted new fields to conquer, or he may have become dissatisfied with the practical working of the English so-called freedom of government. It does not seem likely that the clouds of revolution in France were heavy enough for him to anticipate that movement. Further there is no definite evidence that at that time he was a political revolutionist in any sense of the word, although he may have been

a trouble maker in the scientific world.

The immediate cause or opportunity that led him to France was his appointment as Physician to the Body Guard of Comte d'Artois, the youngest brother of Louis XVI. This position was quite attractive. It gave him an opportunity to reside in Paris, to meet the higher classes of society, and to carry on a private practice since most of his time was free. In view of his later democratic tendencies, it is interesting to note that at this time he was quite anxious to establish a claim to nobility. He maintained that the nobility of his family was established in Spain as well as France. His claims were not promptly met and he advanced the further argument that considering his position at court it was honorable for the state that his rights to a patent of nobility be promptly recognized. His plea was never answered but he was given the right to use with his name a mark of distinction corresponding probably to "Honorable" or "Esquire". Strange to say this disappointment apparently did not cause the bitterness that might have been expected. One can hardly refrain from wondering, however, how the revolution might have been affected had Marat been a member of the nobility rather than of the masses.



Marat, the Scientist and Investigator.

His success as a physician was rapid and he soon became known as "the doctor of the incurables". One case that gave him considerable reputation was that of the Marquise de Laubespine. She was rapidly failing with an advanced case of tuberculosis. When called to see her it is said that he examined the expectoration most carefully; unfortunately what he looked for or what he found is not recorded. He promptly discontinued the treatment she had been receiving which was the usual purgation by an extract or soup of snails and frogs. In place of this he substituted general therapeutic measures, rest, outdoor life, vegetable extracts (from such as yarrow plant), balm of mint, balm of tolu and, most important of all, his secret nostrum. His patient made a splendid recovery, as attested publicly by her husband and the Marquise is reputed to have been Marat's mistress for some time afterwards. This, by the way, is the only hint of any loose living on his part.

The use of his secret nostrum in this case and others probably gave rise to the charge that he sold patent medicines at one time. He refused to make public the composition of this nostrum but it was finally analyzed by an Abbé who announced that it proved to be only chalk in water. We do not know whether Marat considered this as a *placebo* or whether he actually believed that the calcium content of the lime in the chalk was of benefit in controlling the tuberculous extension.

His medical publication in Paris during this time consisted practically entirely of case reports, notes and letters. In giving case reports he did not mention the name of the patient, as was usually done, but gave only the initials, remarking that discretion is one of the duties of the physician. From one of his notebooks (not circulated during his life-time) we can read, ". . . My knowledge of nature gives me a great advantage; the rapidity with which I observe, my certainty and tact and my many successes have caused me to be called 'The Physician of the Incurables' ". In discussing medical treatment by electricity he stated: "One must not treat cases except those in which the diagnosis is well established and those conditions in which the disease does not terminate by some natural crisis. It is not sufficient to know how to turn the handle of an electric machine, but necessary to know the mechanism of what one is employing as well." Good advice even today.

The fame resulting from the case of the Mar-

quise, previously mentioned, caused many to demand consultation by letter. Marat advised these to retain their local doctors, observing that physicians who endeavor to practice by mathematical formulae and not according to principles are not pleasing in that they cure few and kill many. He urged that direct examination of patients was much to be preferred.

His fees in Paris varied from five to one hundred and eighty francs. He was evidently a good manager for when about 40 years of age (1783) he practically retired from practice as a wealthy man. Although some discredit the last statement because he died practically penniless, we must remember that the last ten years were unproductive of any income and that in addition to his living expenses he financed his experiments in physics and the publication of several journals.

In 1780 he published a paper entiled "A Plan of Criminal Legislation". This like the earlier "Chains of Slavery" was an innocent political paper showing no signs of revolutionary tendencies. In it he advanced the thesis that crime was a comparative relative act and that medieval styles of punishment, e. g., torture, burning, mutilation, etc., should be abolished. He gave also further evidence that he was not a debauché by his dissertation of crimes against sexual morals and stated that he believed prostitution could be cured by relieving underlying poverty. At about the same time he wrote an article on aeronautics—the occasion being a balloon accident.

Shortly before these two latter papers his interest in the study of physics had increased and continued to afterwards. In fact, his remaining scientific publications were limited to that subject to the exclusion of medical papers. A most important one, appearing in 1779, was entitled, "Discoveries Concerning Fire, Electricity and Light". This was the result of numerous experiments he had done on the nature of fire, which he believed was an ignited fluid. In developing this theory of igneous fluid he almost discovered that heat is motion, as can be judged from the following passage: "Since it is only by penetrating bodies, that is to say, by causing agitation in their tissues, that the igneous fluid dilates them, volatilizes them, (and) consumes them, it is clear that it acts upon them only by the movement of their globules". He argued further that the igneous fluid had weight since heated bodies grow lighter as they cool; and that the igneous fluid is compressible and non-elastic. This paper addressed to the Academy of Sciences of Paris aroused much opposition and was not accepted. This opposition was, however, by no means unanimous as some of the comments show. One stated, "He has furnished a means by which a great field of new research has been opened in the domain of physics;" another, "His experiments have been well made and well demonstrated," and another, "This clever physician has opened a vista altogether new by a method of which he is the inventor and which he has employed with great success". (This last reference is to the use of a solar microscope and dark chamber.)

In the following year, 1780, he offered his essay on "Physical Researches on Electricity", but was still unable to secure recognition by the Academy. It was a characteristic of Marat's to thrive on opposition and in his quarrels with the Academy he well held his own. Once he stated, "A man of genius need not seek recognition of such an assembly because he disdains intrigue and mistrusts the judgment of a coterie," and again, "The Academy has met 11,400 times, has published 308 eulogies and has given 3,956 recommendations. These include pomades for the hair, plasters for corns, ointments for the itch, toupés, syringes, canules and a thousand other objects of equal importance."

As a physicist he unsuccessfully refuted the theories of Newton and Franklin but in his researches on electricity he was quoted and his name frequently cited with those of Priestly, Boyle, Cavendish and others of like standing. Franklin and Goethe praised his labors and Lamark, the naturalist, accepted his views. His works were translated into German and praised by the Dutch and Swiss. He was offered an opportunity to work under the patronage of royalty at the court of Russia but refused. His work on electricity continued almost up to the time of the revolution for in 1786 he published "Fundamental Ideas on Optics" and " Memories of Medical Electricity". This latter was in answer to this subject, "To what degree and under what conditions can we count on electricity—both positive and negative —in the treatment of disease". His essay, which did not give unqualified approval to all cases, was "crowned" by the Academy, not of Paris, but of Rouen.

During the height of his unsuccessful quarrel with the Paris Academy, he attempted to secure appointment as head of the Royal Academy of Sciences in Spain. In his correspondence occurs the rather amusing phrase, "My heart has long been Spanish." Here, again, he met only disappointment. He was gradually becoming embittered, he lost interest in science and his mind became fertile soil for revolutionary ideas. In this way, there was a slow but definite change and Marat, the scientist, aristocrat, lover of nature, author of discoveries in physics, physician, and writer of philosophical and literary works was gradually submerged and Marat, the "Friend of the People", a fanatical journalist, pamphleteer, and demagogue arose in his place. While our interest is primarily in what has just been discussed let us briefly follow his career in the Revolution.

MARRIAGE

At the beginning of his political career his publications were so radical that he was compelled to live in hiding and soon came to want. It was

then in 1788 that he met Simmone Evrard, who even before she knew him, had admired the patriotism and fire of his writings. She found him in financial distress, discouraged and ready to return to England to resume the practice of medicine. Although she was twenty years younger than he, a firm attachment resulted and she became his common law wife, the only marriage ceremony being the one described as follows: "On a beautiful day Marat took Simmone by the hand, together they knelt in the sunlight, while Marat called the heavens to witness that he would never take to himself another wife." Marat kept his promise and according to all accounts they were a devoted couple to the end. Simmone sacrificed her modest fortune and her whole life for him and his cause which she believed in so much. She was never active as a political leader, being content to inspire him and aid in operating his printing press. I could find no record of any children from this union.

Marat's respect for her and his desire to insure her standing is evidenced by the engagement certificate written before a hurried trip to London in 1792, but not found until after his death. It read as follows: "The admirable qualities of Mlle. Simmone Evrard having captivated my heart, whose homage she had accepted, I leave to her as a pledge of my fidelity during the journey I am about to take to London, my plighted troth to give her my hand immediately on my return. If all my affection should not seem to her a sufficient guarantee of my fidelity, let this engagement be forgotten and let me be covered with infamy.

"At Paris, the first of January, 1792. Jean Paul Marat, "'The Friend of the People.'"

Simmone was with him when he died. She lived nearly 30 years longer, most of the time in a garret in Paris with Albertine and until her death in 1822 devoted herself to defending his memory. Surely there must have been something of good in Marat to inspire such an attitude on her part.

RELIGION

While Marat is popularly supposed to have been an atheist and while his "Essay on Man" is frankly materialistic he probably did believe in a God, although he followed no formal religion. He liked Tom Paine's phrase, "The world is my country; to do good is my religion". In 1774 when he became a Freemason in London he certainly must have given some sort of assent to a theological system and belief in a Divinity. Later when attacking the Academy he said, "They have formed the horrible project to destroy all religious order, and to annihilate religion itself." His "Marriage" ceremony, too, might be construed as an admission of belief in a Supreme Being. No reference is found after this to religious views in any manner favorable or unfavorable. It seems likely that he was a deist, that he was tolerant, but that he gradually became almost entirely indifferent insofar as religion was concerned.

APPEARANCE

A description of Marat's appearance has of necessity been delayed until we reach this stage of his career. Historians were not concerned as to how *Dr.* Marat looked, and we can only assume that his appearance during his days of practice was much like what follows except that he was probably more careful in regard to his toilette and his clothes and had no peculiarities due to the skin disease contracted later.

From all description and available photographs he must have been horrible to gaze upon. He was so ugly and ferocious looking that it is no wonder he was called "The Darling of the Scum of Paris". He was a dwarf or bantam in size, being only five feet tall and never weighing over 120 pounds, (I was surprised to read in a description of him that his weight was the same as Shakespeare, whom I thought was much heavier.) Marat's hair was unkept and reddish in color; he had a large bony face. His forehead was large, his complexion was cadaverous, and there was a noticeable scar over his right eye. Both eyebrows were thick and bushy and his yellowish gray eyes were piercing like those of an eagle. One eye, however, was higher than the other, giving his face a lop-sided appearance. His nose was like the beak of a hawk, his thin-lipped mouth matched his nose and his chin argued trouble. Marat's neck was short, his shoulders and chest were broad, and his arms thick. His shirt usually open, revealed a yellow withered skin. The lower part of his body was thin and his legs bowed. He had unusual body strength for his size and always carried a dagger. His long finger nails were filthy. Because of frequent headaches he often wore on his head a handkerchief soaked in vinegar. He always stood on his toes and in walking used a hopping gait with his legs apart. Generally he appeared worried since he was always under intense strain. There was no reference to his teeth—probably because he never smiled. His clothes were ragged and unkept, as was appropriate for one who represented the unwashed. His entire appearance was such as to have been as a strange mixture of the terrible and the ludicrous. The prejudiced Carlyle in his "History of the French Revolution", which is dramatic rather than historical, described him as a "common horse leech, redolent of soot and horse drugs". Marat was not a horse doctor but his appearance must have been terrifying, particularly in anger.

HEALTH

His physical health, and some believe his mental health, were in keeping with his deformed body—especially during the last few years. He always led an irregular life. When writing an article or book or doing experimental work he would disregard the need of both food and sleep, indulging in them only when convenient. His only stimulant was large amounts of coffee. While he tended

bar in his student days he never drank much and most of his life he was a total abstainer. As was to be expected from his habits he suffered from insomnia and as mentioned before had frequent severe headaches. There is no mention of any play or recreation on his part. It is not surprising that he became neurasthenic when one considers the constant drive he was under and the irregular habits he had. Those of us who like to relax at golf may use his example as justification.

The skin disease he suffered has been subjected to many diagnoses: It first appeared in 1788, beginning in the region of the perineum and scrotum. It gradually spread over the entire body and was characterized from the first by an intense itching, relieved only by submerging the various parts in water. It has been described as a lichenoid eczema that assumed the character of impetigo. Carlyle diagnosed it as syphilis, probably basing his opinion only upon the facts that the disease was a loathsome one and that Marat was the victim. Leprosy is another diagnosis that has been made. As his face was involved, it was probably not scabies. Pityriasis has been suggested, but ruled out because the disease first appeared on the perineum. Another diagnosis accepted by many was *dermatitis herpetiformis*. It is reported that he was unusually fond of sweets, which might suggest diabetes as playing a part in the etiology. At any rate he was quite miserable because of it and, I imagine, the perineal irritation may have been responsible for his peculiar gait in walking. In one of his papers he described his health in a general way as follows: "Perhaps some will come to see the dictator, Marat. They will find him in his bed, a poor devil who would give his all on this earth for a few days of health, but always occupied a hundredfold more by the unhappiness of the people than by his own illness."

There is no doubt that he was unusual, and perhaps abnormal, mentally. He was precocious, egotistical, irritable at opposition and inconsistent (probably believing that consistency was the bugbear of little minds). Psychiatrists of repute have classified him as a paranoiac attributing to him systematized delusions of persecution and exaltation. These delusions have been explained as well grounded. He suffered many disappointments and he did have many enemies, their persecution really resulting in his death. So far as exaltation was concerned there is no denying that he achieved prominence in several fields of endeavor and it may have been only his expression of his love of glory which stimulated him all his life. The self-praise in his autobiography, a selection from which follows, may have been only a welling up of repressed emotions. At any rate it is rather interesting. Writing for the Journal of the French Republic, he states, "Born with an impressionable nature, a fiery imagination, a hot, frank, and tenacious temperament, an upright mind, a heart open to every lofty passion, and above all to the love of fame, I have never done anything to pervert or destroy these gifts of nature, but have done everything to cultivate them.

"By an exceptional good fortune I have had the advantages of receiving careful education in my father's house, of escaping all the vicious habits of childhood that enervate and degrade man, of avoiding all the excesses of youth, and of arriving at manhood without having abandoned myself to the whirlwind of the passions. I was pure at the age of twenty-one, and had already for a long time past been given to the meditation of study. The only passion that devoured by mind was the love of fame: but as yet it was only a fire smouldering under the ashes. The stamp of my mind had been impressed upon me by nature but it is to my mother that I owe the development of my character. This good woman, whose loss I still deplore, trained my early years; she alone caused benevolence to expand in my heart. It was through my hands that she caused the succor that she gave to the indigent to pass, and the tone of interest she displayed in speaking with them inspired me with her own feelings.

"Upon the love of humanity is based the love of justice, for the notion of what is just comes from sentiment as much as from reason. My moral sense was already developed at the age of eight. Even then, I could not bear to behold ill-treatment practiced upon another; the sight of cruelty fill me with indignation, and an injustice always made my blood boil with a feeling as of a personal outrage.

"During my early years, my constitution was very delicate; moreover, I never knew either petulance or obstinancy or the games of childhood. Docile and diligent, my master obtained everything from me by gentleness. I was only chastised once, and the resentment at an unjust humiliation made such an impression upon me that it was found impossible to bring me again under my instructor's authority. I remained two whole days without taking nourishment. I was then eleven years old, and the strength of my character may be estimated from this single trait. My parents not having been able to bend me, and the paternal authority believing itself compromised, I was locked up in a room; unable to resist the indignation that choked me, I opened the casement and flung myself into the street; happily the casement was not high, but I did not fail to hurt myself seriously in the fall, and bear the mark on my forehead to this day.

"The shallow men who reproach me with being a 'tete' (obstinate fellow) will see from this that I was such at an early age; but they will refuse perhaps to believe that at this time of life I was devoured by the love of fame; a passion that has often changed its object at different periods of my life, but which has never quitted me for a moment. At five years of age I wanted to be a schoolmaster; at fifteen a professor; at eighteen an author, and at twenty a creative genius. This

is what nature and the lessons of my childhood have made me. Circumstances and reflection have done the rest. I was reflective at fifteen, a thinker at twenty-one. At the age of ten I contracted the habit of a studious life; mental work had become a veritable necessity for me, even in illness, and my greatest pleasures I have in meditation."

Some have believed he was hydrocephalic but their only argument seems to be the size of his head. There were no physical stigmata of acromegaly and his fiery disposition belied a pituitary disorder.

In considering his mental health one must remember that his actions during the Revolution are not necessarily an index to his previous state of mind. Marat was impressionable, and no doubt molded by the circumstances of those terrible times. One has only to consider the World War hysteria of a few years ago to realize that unusual times produce unusual reactions on people at other times quite normal. While it is true he had a violent temper in his younger days, yet some of that may have been an intentional literary style rather than his true disposition. He unquestionably possessed some of the finer feelings as evidenced by his attachment for Simmone and by the following letter written in reply to a request to perform an autopsy on a friend.

"My sensitiveness, my dear Comte, does not permit me to assist at the opening of the corpse of a friend. I shall be represented tomorrow by M. Boyer, Master of Surgery, who will work on the cadaver. He is a very experienced practitioner; he lives at Rue de Bourgogne, two doors from me, at the house of Mme. Vernier. I pray you to invite him tomorrow and mention the hour. It is a favor which I expect from your friendship. Tuesday evening,
(August 23, 1781).

(Signed) "Marat."

Certainly the author of such a letter possessed some sensitiveness and was capable of some degree of affection.

CHARACTER

A consideration of his character is really a continuation of our discussion of his mental health. He was not only a martyr but also had a martyr-complex. Even in his younger days he enjoyed or at least had a morbid expectation of unjust treatment and believed he was being persecuted. His expectations were generally well founded but probably resulted from his fiery bitter and unsocial disposition. He never credited an opponent with honest or sincere intentions, and naturally was suspected by them. In one way he did lack perfect balance in that he could never see the ridiculous side of anything. This is, however, a usual trait in martyrs—in fact it has been said that Lincoln was the only martyr who ever had a sense of humor. Like most conceited individuals he was rather selfish, probably due to his overwhelming ambitions. Marat was intensely emotional, "developing all the strands in his bundle of impulses". Some biographers claim that his influence was derived by overworking his emotions rather than his intellect and that his speeches were examples of "tremendous verbal diarrhea, making use of an overwhelming cataract of talk to give the impression of profound thinking." This may have been intentional for he certainly knew how to handle the mob. It is difficult to accept the view that he himself really believed some of the things he said and wrote. There are, however, two most necessary traits of character which he possessed to the fullest. One was courage, both personal and political—nothing disconcerted him and no danger terrified him. The other trait even more important was strict honesty. While he never had a real sense of justice, no breath of scandal has ever touched upon his financial transactions. Not only did he refrain from graft or confiscation for personal use but further he never received a government salary. So far as his health and finances were concerned his part in the French Revolution was most unprofitable.

POLITICAL VIEWS

In 1789 there appeared his article entitled "His Offering to His Country" in which he depicted the miseries of the people and urged that the National Assembly be called. Later in his weekly journal "The Friend of the People" he presented his "Plan of Constitution" advocating the establishment of a dictatorship. While he loved the common people and was ready to die for them he had no confidence in them and was in favor of dictatorship since he believed that true Republican government was too mature for them to grasp. Danton and Robespierre opposed this since they suspected Marat of seeking the dictatorship for himself. Through numerous articles in his Journal it is seen that his political philosophy is based on Rousseau's teachings. (In fact, one critic states that it is Rousseauism filtered through a paranoic mind.) This philosophy was that government had its permission for existence from the consent of the people, who could take away at any time the power of ruling lodged in a government if that government did not furnish a condition better than that offered by a state of nature. "The people", as Marat insisted, "were those without property and without occupation." They alone, according to his teaching, had the right to rule. He was not interested in the peasants but deliberately cultivated the lower classes in Paris and soon was able to control them. Marat considered himself the savior of these people and imagined himself a political genius, as he probably was. Certainly he could not be called a statesman since he believed that the whole art, craft and mystery of statesmanship consisted in enraging the populace so that they would destroy. "Government by murder" was quite in keeping with his ideas. One

rather doubts Marat's sincerity when he says, "No one abhors the shedding of blood more than I do, but to prevent its flowing in seas, I urge that a few drops be shed." If the French Revolution resulted in the shedding of only a few drops of blood let us hope that none of us will ever see it flow in seas!

Marat's test of patriotism was a very simple one, namely, "If you do not agree with me you are not a patriot and if you are not a patriot you should die." Marat's wrath and executive ability were not reserved for the royalists and nobility exclusively. He was just as bitter against the Girondists who represented the great middle class and who wanted a moderate democracy. He fought them incessantly and when they were in the ascendency he had to hide in the sewers of Paris to escape arrest and bodily harm. It seems likely that were Marat here today probably he would be associated with those favoring anarchy.

REVOLUTIONARY ACTIVITIES

In 1789 Marat was largely instrumental in urging the mob, composed largely of women, to march on Versailles and bring the royal family to Paris.

Subsequently Louis XVI lived peacefully at the Tuilleries Palace and accepted the plan for a limited Monarchy. All differences between him and the National Assembly might have been reconciled had Mirabeau lived. This great statesman died, however, in 1791, and the King again began to show disregard for the peoples' representatives. He attempted to escape from Paris and join the Army of the East which still was considered loyal. Even after his capture at Vareness and his return to Paris the King possessed some degree of power as is evidenced by the dispersal of a revolutionary meeting at the Champs de Mars and the subsequent search for Marat, who again was compelled to hide in the sewers.

The Jacobins or radicals, now led by Robespierre, Danton and Marat, were dissatisfied and organized another body called the Legislative Assembly and a self-organized super-government termed the Jacobin Commune with headquarters at the Hotel de Ville.

War was declared on Austria against the opposition of Marat, who feared that war fever might detract from Republican enthusiasm. Prussia joined with Austria and the Duke of Brunswick, leader of the invading armies, issued a statement that his soldiers were fighting to bring about the restoration of royal authority in France. This led to the Jacobin Revolution; Marat was one of the Committee of Public Safety which had the Tuilleries mobbed and its loyal guard massacred. Louis XVI went to the Assembly for security and was suspended. An executive committee was appointed and a National Convention summoned. Due to the frequent defeats of the French armies duplicity on the part of the royalists was suspected and hundreds of them were imprisoned. Possibly the most cruel phase of the revolution was the disposal of these prisoners in the September Massacre which Marat helped organize if, indeed, he did not originate. After a perfunctory trial the prisoners were told they were "freed" and then released to the mob for wholesale butchery.

At the Battle of Valmy the French defeated the allied forces and the revolution was saved. Had the allies reached Paris, history would have been changed. The National Convention which had been summoned met in September, 1792, and proclaimed a republic. Marat then urged the trial of Louis XVI, guaranteeing protection to the latter's attorneys and insisting that the king be tried only on the charges dating from his acceptance of a limited monarchy. Louis was beheaded in January, 1793; afterwards, steady slaughtering began. As the Royalists were being disposed of Marat turned his attention to the Girondists and succeeded in breaking their power and having many of them guillotined.

DEATH

After the complete rout of the Girondists, Marat resigned his place in the Convention. His health was poor and he suffered intensely from the skin itching which was now quite generalized. Practically all his waking hours were spent in a tub of water across the top of which he had a board upon which he could write. Because of his miserable physical condition and possibly due to some mental deterioration, his writings assumed such a definitely different and peculiar strain that his sanity began to be questioned.

Possibly a more bitter fate would have awaited Marat had not Charlotte Corday appeared on the scene. This twenty-four-year-old girl from the Provinces felt intensely that the salvation of France rested in the hands of the Girondists who would establish a true Republic based on genuine justice. Well aware of the penalty involved, she determined to aid their restoration by disposing of their arch-enemy, Marat—not appreciating the historical fact that the blood of martyrs is the most nourishing of foods for the strengthening of any cause. After purchasing the knife which she expected to use Charlotte Corday had considerable difficulty in gaining an audience with Marat. In fact she was leaving the residence the second time in July, 1793, when Marat upon overhearing the conversation, instructed Simmone to allow the girl to enter his room. She explained to him from where she was and the fact, already known to him, that the Girondists were most active in the Provinces in which her political bias had been nurtured. He promised Charlotte that her enemies all would be killed. As Marat was writing the names which she mentioned she struck one swift blow with the dagger. In a few minutes Marat was no more. Perhaps there was never a more accurate blow struck than that blind stab. The autopsy held on the following afternoon by

Louis Deschamps, Chief Surgeon of the Charity Hospital, confirms this statement.

REPORT OF NECROPSY

1. "External Examination—I observe at the superior and anterior surface of the chest, near the sternum on the right side, a transverse wound, slight, oblique, about six lines in length. The surrounding parts are blood-stained.

2. On opening the abdomen, I observe an adhesion of the portion of the intestine with the peritoneum; for the rest, all the parts in that locality are in a healthy state.

3. I examine the viscera contained in the chest. I note that the right lung is adherent to the pleura throughout its external surface. The pericardium is opened, it is filled with a quantity of coagulated blood; the aorta near the beginning of its curvature has been pierced through and through; at the lateral wall is a pouch quite close to the apparent origin of the heart. The left auricular appendage has been penetrated near its base; the right lung is a trifle pale, its superior extremity was pierced throughout its thickness. The left lung appears to be in its natural state.

The results of my observation are, that a piercing, cutting instrument directed from before backward, from right to left and from above downward, entered the chest; in the course which the instrument followed, it entered the chest between the first and second ribs, traversed the superior part of the right lung as well as the aorta and entered the left auricle of the heart.

4. On opening the cranium, I have found the cerebrum and the cerebellum in their natural state.

Done at Paris on the said day and year and
Signed at the present *process-verbal*,
DESCHAMPS."

The effect of the murder of Marat was electrical. The masses which had been turning against him began to idolize his memory as had never they done even in his prime of influence when alive. Streets were named for him. His name was adopted by many, even, it is said, by Murat, later one of Napoleon's most competent leaders. He is reported to have changed the spelling of his name, substituting an "A" for the "U". Charlotte Corday was, of course, promptly executed, her so-called trial being only an attempt to compel her to name her confederates and to describe how she had acquired such skill with a dagger.

Early putrefaction compelled the burial of Marat's body after it had lain in state but two days. In accordance with the will of the populace, the Assembly voted to "Pantheonize" him, and in order that his might be the first body in the Pantheon, that of Mirabeau who had preceded him was removed. Marat's heart was placed in a separate container and maintained as a shrine. It seemed that Marat had been one of the few fortunates (so far as history is concerned), who have died at the right time and in the right manner. While the path of glory had led him but to the grave, it did appear to be a most glorious grave.

Before long the uncertainties of even death appeared. Marat's enemies gained the ascendancy. In January, 1795, one of his earlier writings, the "Plan of the Constitution", was interpreted as monarchial. Feeling ran against his memory. When the discussion was at its height his widow, Simmone, appeared before the Assembly and delivered a wonderful tribute to Marat's memory, saying in part: "Citizens, you see before you the widow of Marat. I do not come here to ask your favors, such as cupidity would covet, or even such as would relieve indigence; Marat's widow needs no more than a tomb. Before arriving at that happy termination to my existence, however, I come to ask that justice may be done in respect to the memory of at once the most intrepid and the most outraged defender of the people. . . ."

The widow's efforts were in vain; Marat's body was removed from the Pantheon, his heart thrown into the sewer in which so often he had hidden, and he was denounced as a monster. His widow and Albertine continued to struggle for his honor, but it was years after their deaths before there was any official kindness exhibited towards his memory.

SUBSEQUENT PROGRESS OF THE REPUBLIC

After Marat's death the Reign of Terror continued to widen its range among many others. Marie Antoinette was killed, Danton, the associate of Marat and of Robespierre, was guillotined and French armies invaded all of Europe endeavoring to spread freedom and liberty. Hebert and his party of atheists who had proclaimed the Feast of Reason, lost favor with Robespierre and were killed. Finally, Robespierre himself antagonized the Convention, was captured from the Commune where he had sought safety and then himself was guillotined within less than a year after Marat's death.

The Reign of Terror ended. The Convention appointed a ruling directory of five; this later was superseded by the three consuls, one of whom was Napoleon Bonaparte, who had distinguished himself in recent military operations. He became First Consul and then Emperor. The wheel had turned and the First French Republic disappeared, but the fruits of the Revolution still are apparent.

SUMMARY

We hold no brief for Marat. Probably no amount of whitewash could ever make him a character to admire. While we are not at all in sympathy with those who excuse most criminality on the basis that it is due to heredity or environment of both, nevertheless we feel that in the final analysis of Marat as a man, many factors must be considered. In spite of his appearance (as depicted by some of his photographs) and in spite of competent opinion to the contrary, it seems to me that the man was sane. We believe, too, that inherently he was not cruel. (The fact, frequently overlooked, is that there was practically no torturing done during the Revolution.) Instead of considering Marat abnormal, we would consider him a normal, or at most an unusual man living in and affected by most abnormal times. Certainly he was no worse than were many of his

associates. If he was more prominent it was because of his ability to control the mob which was the ruling element during the Revolution.

Marat was egotistical, selfish and intolerant even in his better days, but so are many individuals, even now. Most of us who are frank will admit that luck or fate plays a prominent part in one's existence. How often has not some insignificant or at least unplanned-for event changed the course of our lives. All of Marat's luck, so far as avoiding participation in the Revolution, was bad luck. Had he been contented in England, had he acquired his patent of nobility, had he obtained recognition by the Academy in Paris, had he accepted the appointment to the Court in Russia, had he secured the position as head of the Royal Academy of Spain or had he not met Simmone when he was about to return to practice in England, his name probably would be unknown or at least not associated with the Reign of Terror. His bad luck continued even after his death since it is only rather recently that anything good had been said about him.

If a man's historical importance is determined by the number of people whose lives have been influenced by his activities, Marat's place in history is secure. Nothing anyone may say can alter that fact, but we believe that an appreciation of his sordid temperament, his disappointments and his revolutionary environment should lead to a more kindly feeling towards his memory.

The thought occurs in closing that many of Marat's difficulties might have been the result of unusual intellectual achievements which far surpassed his ability for social advancement. In other words, did he have that ugly streak of intolerant positiveness, often seen in the lower classes, so firmly attached to his makeup that his demands for recognition served only to arouse opposition? How unfortunate for Marat if his disappointments and bitterness were the result not of what he *did* but in the *way he did it!*

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NOTICE

The demand for back numbers of this journal has been so unexpectedly large that the publisher is left with only enough on hand to fill orders for bound volumes. To those subscribing to the Journal, it will be encouraging to learn that the publishers are considering planographing all previous issues into an inexpensive edition, provided sufficient demand continues to be evident.

—Sandfield Publishing Co.

SECTION XI—*Societies, Programs and Proceedings*

The History of the New York Gastroenterological Association*

By

ANTHONY BASSLER, M.D.
NEW YORK CITY, NEW YORK

PROGRAM

Commemorating the 100th meeting of the New York Gastroenterological Association, Union Club, New York City.

History of the New York Gastroenterological Association :: Anthony Bassler, M.D.

History of American Gastroenterology
Col. Fielding H. Garrison
Medical Corps, U.S. Army

Through the Alimentary Canal with Gun and Camera :: :: George S. Chappell
("Capt. Traprock")

CERVANTES has said: "History is the depository of great actions, the witness of what is past, the example and instructor of the present and monitor to the future." Nineteen years ago the founders of this organization conceived a picture; today it is painted. It might be well tonight to look at it because the picture that was started and today is finished by us is a subdued one, rather than one with variant colors striking to the eye. Instead, it is one striking to the mind, and useful to the subject and to medicine.

In this picture it was decreed that there were to be no rancor of politics, no uncertainty of the minds of the multitude, no avenues for men for self-purposes, no place to please one's friends or perplex one's foes, no place to squander words for fame. When this picture was started, we wrote a prayer of faith, and today we are still saying it. It is said that prayers never come creeping home. Yet, we have continued the one which we started with. We began in the days of opprobrium of gastroenterology due to errors within ourselves. The knowledge of these and their correction brought an appreciation of the definite trends and the development of research attitudes, better clinical work, advances in physiology, surgery, in the X-ray room and in laboratory. We chose the latter and designed a Forum to keep our perspective on the rapidity with which the future history of gastroenterology would fuse.

In all of this it seemed that an organization in which the men of New York City could assemble amid those God-given gifts to man of friendship, sociability and hospitality and in each other's homes, as different workers could make known their experiences and exchange ideas, the effort would be worth while. It was foreordained in principle not to have set papers, but to meet among ourselves in a sort of "round robin" way, isolated from the profession at large, in a sort of court of free discussion. We held that we should keep free from aggressive self-assertion born of competition and the desire to make the most of oneself, still too commonly seen in large medical gatherings. Rather, we bound ourselves in that atmosphere of humility which comes from the reverence for truth and proper estimations of the difficulties encountered in the search for it. We started amid the cocksureness of opinion which we had seen in others, and were guilty of ourselves and which leads to conceit. Steadily we have held to the conviction that absolute truth in our work was hard to reach, that slips even in the best of us were inevitable, that errors in judgment must occur in the practice of an art which consists, as Osler has so well put it, "in the balancing of possibilities". We began and have consistently maintained the slow process of guarding against self-deception by a healthy criticism so we could see and value the truth, and draw from our own errors the lessons which all would be enabled to be strengthened by. These prayers have been held inviolate and the history of this organization suggests they are ineffaceable. Your founder and first president gives thanks for them and joins with each of you in the happiness of their consummation.

As I look back over the years of this organization, I see nothing to reproach ourselves with, and we are too modest to cheapen it by praise. Horace has said: "What's well begun, is half done". As you know, the beginnings of most things are small; commonly men lose sight of the goal for which they started. The first was true,

*An address delivered on the occasion of the Celebration of its *One Hundredth Meeting, October 11, 1934.*

the second did not happen. Before our time, there was a proprietary society of gastroenterology in New York City run by the late Doctor George D. Lockwood. The meetings were held in his home, at his call and the membership were those he invited to the gatherings. It is long since out of existence. Our organization was begun by a few men who responded to the call for the establishment of a real organization, one free from personality of any sorts. From this nucleus, characterized by certain principles and beliefs, the organization grew, slowly, definitely and deep in the purpose of exchange of knowledge. From inspiration there developed reason, finally custom and continued procedure. Guiding these have been the presidents: Bassler, Roberts, Bastedo, Hayes, Brooks, McWilliams, Stewart, Lynch, Holland, Woolsey, Crump, Andresen, Le Wald, Yeomans, Eastmond and Anderton, and the secretaries: Stewart, Eastmond, Andresen, Lutz and Kantor. But to none of these can solely be given the credit for its success. This was inherent in the members who carried the original principles onward, and who undertook to preserve in their meetings the noblest attributes of the physician: character, humility, humanity, modesty, integrity, ideals, progress and toleration. I have never seen jealousy, intolerance, insincerity, pedantry, politics and prejudice raise their heads among us that the individual did not learn that these were not in the tenets of the organization. From the sidelines I have watched some of our new members schooled in papers for open types of medical meetings, soon build up into the modest and noble, and I doubt that I shall ever cease hearing expressions of happiness and values of our members for belonging to the organization.

As to the good that we have done medically, who can value that? Yet, I feel sure, that by our meetings we have served a useful purpose to better understanding of subjects, to making us more worth while as gastroenterologists, and to the profession and public. Without intending to be personal, it is my observation that when a subject has been thrashed out among us it often occasions surprise to hear it presented by someone outside. Ofttimes, in other than our own meetings and in meetings held outside New York City, I have wished that the records of a discussion by us on the same subject could have been used instead of the programs that were offered. This is not said in egotism or even a sense of pride. So as not to be personal, ask yourselves if this has not also occurred to you. There are times I feel that our discussions of a subject should be published. On this, though, I wonder that if they were, would they be as frank and candid as when we engage in them behind closed doors? It is difficult to dampen the human effort made outside with the temperance of heart and soul so conspicuous when among ourselves.

Tonight we celebrate the centennial meeting of the organization. It is not necessary to record the long array of subjects discussed or the many new ideas and advances that were born among us. Many from the outside we have nourished to fruition here, others were seeds of ours that blossomed elsewhere. We are modest in the virtues of our achievements, hoping we shall be the better liked for it. Henry Ward Beecher once said that self-contemplation is apt to end in self-conceit and we do not wish our scale brought down by such a fault, especially in that it is so foreign to our desires and policies. The historians of medicine usually present the great things that have occurred or the personages involved in them. Many that have been discussed among us are important, but in building up the fabric of gastroenterology there is much weaving and warping, thousands of details and each one of them important to have knowledge of. It is for these particularly that we meet and we have been blessed with a wise handling of them. Their record in the files of the association is long, too long to mention, and rather than mention a few and leave out the important rest, we give homage to them all. In the hours that it takes to peruse the records, it shows that practically nothing has escaped us, and nothing from the outside has missed our scrutiny and effort. The record from the beginning up to today is essentially the history of gastroenterology during the years that we have been in existence. Not that from our organization have come the most important of these, but that from whatever source including our own, they have had most analytical attention and the freest type of discussion. No one can go over the records and not be definite in the thought that the part in gastroenterology that this organization has played was well done and useful and for our future we could not ask for more.

Recto-Sigmoid Cancer with Acute Gangrene of Pelvic Organs

By

CHARLES E. HOWARD, M.D., F.A.C.S.
CINCINNATI, OHIO

CASE REPORT

Jewish Hospital, Case No. CC713, T. S., white male, single, age 52, mechanic. This man was admitted to the clinic service March 2, 1933, acutely ill.

Chief Complaint—Pain in the pelvis and marked constipation.

Previous History—Patient states that he has always been in good health. At the age of 30 he was operated for hemorrhoids. One attack of pneumonia in 1919.

Onset Present Trouble—For the past ten months he has noticed an increasing constipation. About the middle of January, 1933, he experienced severe pain in the pelvis and passed large amounts of mucus and bright red blood. His family physician advised enemas of mercurochrome, which he states stopped the bloody mucus. Pain continued. He shortly began to notice what he called "shreds of skin" in the stool. Patient ate less because of the extreme distress at stool time.

Condition on Admittance—A well-developed, poorly nourished and emaciated white male with an anxious expression. Temperature, pulse, respiration and blood pressure within normal limits. Chest negative, abdomen distended and tympanitic. Patient complained of pain in the upper rectum, back and abdomen. States that he passes large amounts of mucus, blood and necrotic material. States that he has had no real bowel movement for eight days. Admits marked loss in weight. Claims to void without difficulty or frequency.

Proctologic Examination—Digital negative. Eight-inch proctoscope reveals a narrowing of the recto-sigmoidal juncture, through which a small amount of blood and mucus pass. It was impossible to secure an excellent view of this area, because of the marked narrowing of the lumen and the angulation. The mucosa slightly within the strictured area was inflamed and thrown into little polypoid-like masses. Two of these were removed for section. The pathologist's report was negative for malignancy. This report was discounted because we were unable to get a section from a proper area.

X-ray Examination—Gaseous distention of the large bowel. A large deformity in the recto-sigmoidal area with marked stricture opposite the sacral promontory. (See Figures 1 and 2.)

Preoperative Diagnosis—Recto-sigmoidal malignancy with marked stricture, impending complete obstruction.

Laboratory Findings—Urinalysis normal except for small amount of albumin, reds 4,000,000, whites 12,600, hemoglobin 80 per cent, Wassermann negative, blood sugar 116, nonproteid nitrogen 32.

Operation—March 10, under general anethesia the lower abdomen was opened with the midline incision, with the intention of exploring and establishing a permanent colostomy, and if possible to do the abdominal por-

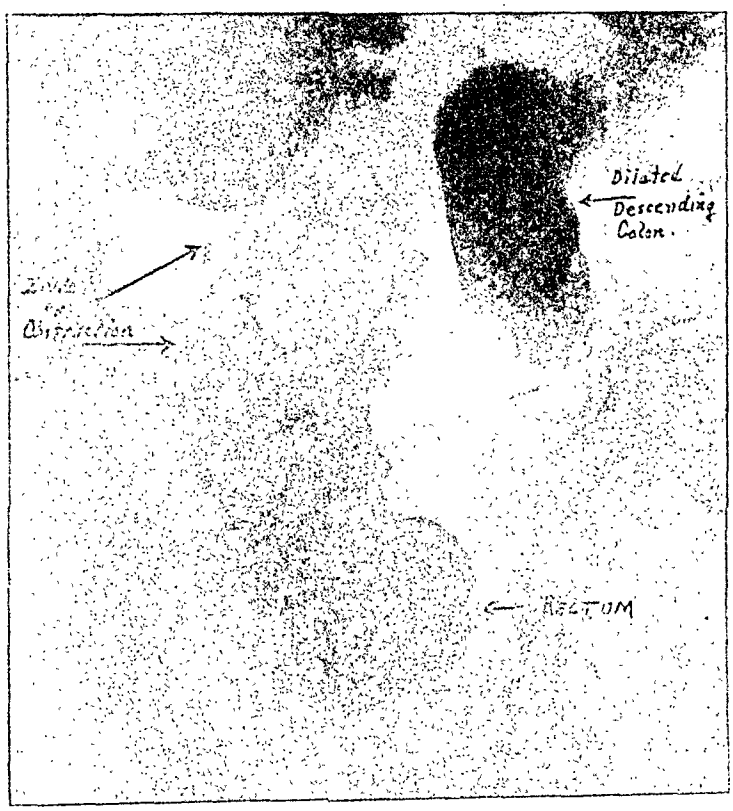


Fig. 1. X-ray demonstration of the zone of constriction.

tion of a combined resection. A very large mass involving the lower sigmoid and upper rectum was found, which almost completely occluded the pelvic strait, was densely adherent to the sides of the pelvic brim and posteriorly to the spine. It was impossible to slip the fingers below the mass anteriorly to the proper depth of the peritoneal reflection. There were no metastases discovered in the omentary or the liver. Believing that a thorough removal was impossible, a fairly high left-sided colostomy was made. The following day a small tube was inserted in the extruded bowel loop and two days later it was widely opened. The patient seemed to improve. Abdominal wound healed by first intention. We were thinking of discharging the patient as incurable, when he suddenly became toxic, semi-delirious, with a temperature ranging between 99 and 102 degrees F. On April 3, a "blister" developed just above the symphysis in the midline healed wound. This rapidly opened and exposed a fairly deep necrotic ulcerated area, which continued to increase in size. There was a discharge of necrotic tissue from this ulceration and also from the anus. About six days after the development of the "blister" there was a copious and free discharge of liquid from the ulceration; this undoubtedly was urine. Patient up to this time had voided normally. From then on, no urine passed in the natural way. On April 10, the patient died.

Pathological Diagnosis — General low-grade peritonitis, general, acute necrosis of all pelvic organs. Toxic liver, kidney, spleen and heart. No gross evidence of malignancy found. The sigmoid and rectum, the bladder and prostate and seminal vesicles all were anatomically destroyed. About three inches of the colon of the lower arm of the colostomy was all that remained. A small piece of tissue was found in the pelvis, which, upon section, proved to be a piece of the prostate; this exhibited definite malignancy upon microscopic examination.

Comment — The pathologist was of the opinion that the condition was a primary cancer of the prostate with subsequent involvement of the bowel. To this I could not agree, because of the lack of urinary symptoms at any time prior to the terminal episode, because of the definite history of primary bowel trouble, the proctologic, X-ray and operative findings. It is my opinion that at the time of operation at least one ureter was involved and that later ulceration permitted the escape of a small amount of urine into the growth, which rapidly caused the progressive and enormous necrosis noted. One must, however, bear in mind the possibility of extensive interference with the major blood supply to the pelvic tissues due either to direct pressure of malignancy upon a great and essential artery or to the formation in a pelvic blood vessel of a thrombus, due possibly to malignant disease or to changes in the intima which permitted a "bland" thrombus rapidly to form. From such sources, general necrosis of the pelvic tissues proceeds with astonishing speed and what a few hours even, previously, had seemed to be a condition of distress due to a chronic, slowly-progressive ailment, quickly exhibited manifestations of an acuteness and seriousness for which physician and patient alike were unprepared.

It is evident from the instance cited that prognosis of necessity must be guarded when at an operation of colostomy to relieve bowel obstruction, a pelvic mass of such extent is encountered that it can be neither thoroughly explored or removed. Perhaps, as surgeons, we have neglected to appraise properly the vascular damage—particularly circulatory blocking—which a rapidly spreading neoplasm is capable of producing, and in a brief time-period.

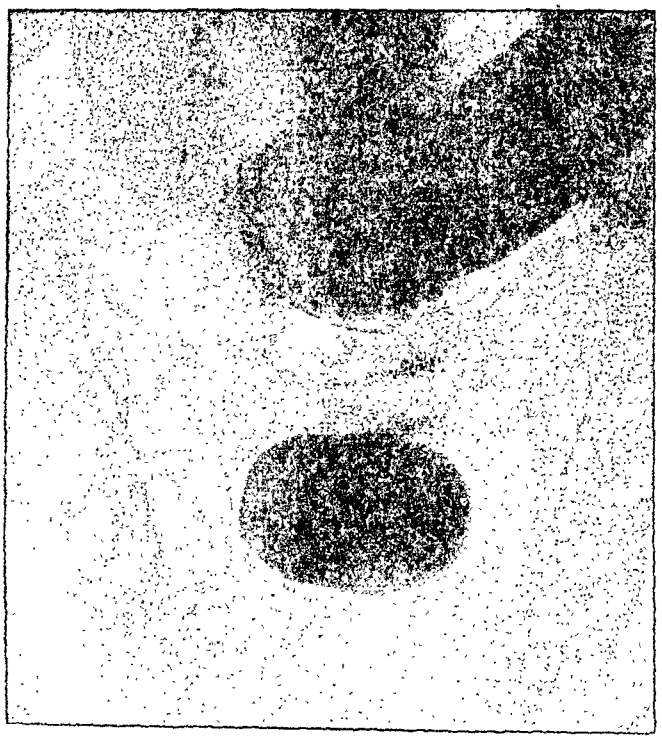


Fig. 2. Further demonstration of the constricted zone, showing dilated colon above.

Readers are invited to submit accounts of interesting clinical experiences

An Instance of Uncontrollable Vomiting of Long Duration: Advanced Malnutrition: Hysteria: Metal Poisoning: Recovery

By

FRANK SMITHIES, Sc.D., M.D.
CHICAGO, ILLINOIS

IN THIS issue there is summarized an important set of studies on so-called "functional vomiting" by Drs. Drenckhahn and Wilbur of the Mayo Clinic. The facts which these observers have emphasized in respect to the frequency of the affection, its differential diagnosis and treatment well are worthy of consideration.

Within the experience of all practitioners have arisen instances of persistent vomiting due to obscure or unprovable causes. It is not necessary here to mention how frequently such patients have been subjected to "exploratory" laparotomy. Often the results have been negative with regard both the discovery of significant pathology or favorable post-operative course. Within the past fortnight, such a patient (aged 27) consulted me who, for the relief of vomiting, has experienced six abdominal operations during a period of less than three years and who yet remains incapacitated by irregularly recurring "spells" of prostrating emesis. Her appendix, gall bladder, uterus, one ovary and tube (apparently all normal, histologically) have been removed; the left kidney has been "taken out, something removed and then the kidney replaced" and, on two occasions, surgical treatment for "dense adhesions" has been exhibited. This unfortunate woman, nervously and physically, is in a deplorable condition, her bewildered husband—a divinity student—has starved himself to dangerous limits in order to pay hospital and doctors' bills and what perhaps is most tragic, his faith in our profession and even in the Deity in whose service he plans to devote his life, gravely is being strained. Certainly the experiences of this young couple have been trying.

The above is not an isolated or unusual instance as the records in many physicians' practices, of clinics or hospitals readily demonstrate. It is not comforting to the members of our profession whose consciences not yet have atrophied or even of those whom the past five years of economic depression have made "careless", to contemplate how many thousands of normal appendices and gall bladders have been removed; "floating" kidneys anchored, "adhesions" (often, indeed, harmless affairs, *residua* of developmental processes) have been severed, gastro-enterostomies performed to relieve "non-emptying" or ptosed stomachs, or, more radically, partial gastrectomies or even resections of "kinked", "twisted", "redundant" or otherwise "potentially obstructive" bowels have been done—and all to no purpose. Heartless though it may seem to state, fortunate have been those psychoneurotics who, in their persistent search for relief *via* surgery, to the utter neglect of such methods of study and management as are outlined by Drs. Drenckhahn and Wilbur, have dared to explore too far the surgical highway and have perished. One needs but recall the delights arising from self-punishment as exhibited by the ancient "Flagellantes", to appreciate how closely allied to them is the psychic comradeship of modern neurotically unstable patients whose persistent vomiting excuses from certain demands of life and to whom the agonies possible from extensive surgical maneuvres add comforting, if painful, thorns to the crowns so acceptably worn.

The patient briefly below reported, from my records, presented certain similarities to those individuals considered by Drs. Drenckhahn and Wilbur, yet, superimposed upon the psychoneurotic make-up, was a deliberate, persistent and cunning degree of deception which made for an interest far greater than is common towards this type of patient. Certainly, only an accidental and happy combination of circumstances made possible a correct diagnosis and led to successful treatment.

CASE REPORT

Miss Dora B., age 18, single, farmer's daughter, seen in consultation with Dr. H., of Y., Michigan.

Major Complaints—"Bilious" vomiting, constant daily and for nearly four months' duration; loose stools; anemia; loss of weight (72 lbs. in about three months) and strength; swollen joints; neuritis; beginning mental confusion; "sore" mouth.

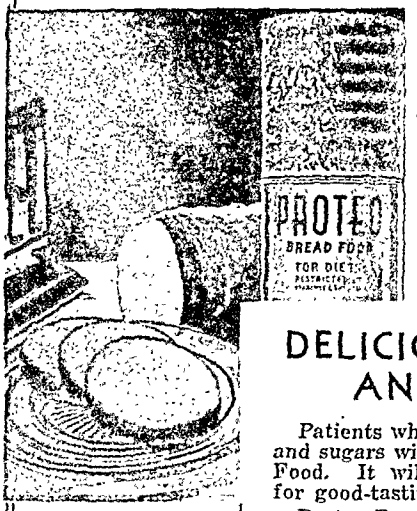
Past History—Usual children's affections; tonsils removed at age 13; otherwise had been a strong, robust, well-nourished, cheerful girl until about age 15, when had some sort of acute, febrile ailment diagnosed "brain fever". Patient had an excellent record in the grade and in the high schools; had had one year at a nearby normal school; always very conscientious about studies and very ambitious. Although at age 16 weighed 156 pounds (height 5-6) and of athletic type, never engaged in sports; made few friends; worked hard about house and farm and even though parents were exceedingly prosperous German farmers, in addition to carrying a heavy schedule at normal school was expected to do as much housework as a "hired hand"; little social life; no vacations; summer school recesses meant only added physical labor due to large family, care of hired hands and the many demands of a busy, well-ordered, successful farm. At rare intervals when

had leisure, usually read rather "heavy" books or did needlework. During past two years had been much concerned with religious matters; parents almost fanatically religious but hard, unsympathetic, thrifty and saving, so much so that when patient completed first year at normal school was told that she had had all the education her parents were going to allow her, that more help was needed at home and since she was a strong, capable young woman, she would have to share the labor.

Although the patient's parents knew of her having had no love affair, rather grudgingly they admitted that they desired her to marry an only son (aged 31) of a wealthy neighboring farmer and that one of the reasons why they wished the girl at home instead of at school was that she would become more efficient as a housekeeper and would be thrown into more intimate contact with the man whom the parents had selected for her to marry. This man, Dr. H. stated, privately, was unattractive and bore the reputation of being exceedingly "close"; he was madly in love with the patient but his affections had not been reciprocated: in fact, Dr. H. stated that it was his opinion that the patient secretly had been "keeping company" with a very popular young Irish Catholic whom she met at school (the patient's parents were rock-solid disciples of Martin Luther and held all the prejudices engendered by the famous Diet of Worms). Dr. H. stated that about six months prior to our consultation the patient had called at his office for treatment of a "cold", had appeared, for her, unusually nervous, seemed fearful of something and had talked at length about religious matters and marriage—the physical aspects about which she was unusually immature for a modern normal school pupil. Dr. H. could elicit no hint of indiscretions of conduct from the girl; in fact, she was kept so busy at home and at school that he could not imagine when opportunity for any sexual or amatory philandering could have been possible.

Present Illness—According to the patient's parents, when, at the opening of the fall term at the normal school (late September) the girl realized that she was not to return, she became moody, had frequent outbreaks of weeping, grew untidy in her appearance and dress, had fits of violent temper and, as the mother said, her "whole nature changed"; she refused to eat and in a few weeks began to vomit, even though but very light diet, chiefly milk, was taken. She had no complaints of pain or other disability. From the first the vomitus was green—"bilious"—at first scant but before long copious; several times daily vomiting occurred. Simple household remedies were of no avail; the patient lost weight and strength rapidly, became pale and languid, stools were loose and later joints of fingers, wrists and knees became swollen; the hands and feet became tender to touch, the urine scant and within a month, mouth and throat were so sore that food ingestion was difficult. The patient became bedridden but not until that time was Dr. H. called. His examination proved negative, but he suspected some organic disease which not yet had advanced sufficiently to permit diagnosis. Remedies to relieve symptoms were prescribed and the physician saw the patient about once weekly. There was no improvement: in fact, after the Christmas holidays, vomiting, weight loss, prostration, joint swelling, anemia and lassitude became more marked. About the end of January, *herpes labialis* appeared and remained fairly constant: the patient exhibited periods of "stupor"; the vomitus constantly was "bile green"; blood-tinged at times and thick with mucus; the stools were loose, often blood-tinged, their passage sometimes preceded by cramp-

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like pains and, even though the patient largely was on milk, cream and soup diet, undigested food-flocculi grossly were visible in them. Menses continued regular; urine was scant and had contained small quantities of albumin and, at times, traces of blood and a few casts. During the week preceding our consultation, the gums had swollen and toothache required relief by *Tr. opii. dcod.* Several small bed sores appeared on the *ischii* and there was a peculiar foul ("dead", as the mother described it) odor about the patient even though she had no incontinence of bowels or bladder. "Mental deterioration" advanced rapidly, the religious ecstacy became pronounced: in fact, only when the local pastor visited did the patient arouse herself; on such occasions, she became voluble. In spite of swollen joints, tender hands and feet and physical weakness, the patient was able to move about in bed, hold a glass when drinking and take care of herself when vomiting or having bowel movements. For convenience, a "back-parlor", giving off the dining room, had been transformed into a bedroom and because of the exquisite sensitiveness to the weight of bedclothes and only a sheet being possible as covering, an ancient stove had been installed so that the large, high-ceilinged, old-fashioned chamber could be kept warm.

EXAMINATION

Made at 3 P. M. of a cloudy, sleety winter's day and by lamplight. Patient a rather strikingly handsome blonde, but so malnourished and pale that she seemed "all eyes"—large, blue, sunken, staring, surrounded by deep rings of tan-brown pigmentation. Although conscious, she answered only in whispered short sentences but, so far as eyes and expression were concerned, appeared quite alert: lay in passive dorsal posture, without dyspnoea; weight loss marked over skeletal muscles but face faily full; crusty *herpes labialis;* slight cough and throat clearing; fingers and wrists seemed stiff and soft parts somewhat swollen; slight swelling at knees and elbows; pallor without icterus. Complaint of nothing but tender hands and feet and nausea; occasionally regurgitated small quantity of rather gross-green fluid, intermingled with milk curds. A peculiar odor—"musty" or "mousey"—was noted even in that large, damp room with its old-fashioned windows, creaky floor and mail-order house, dark green wallpaper, where the atmosphere, normal to the place, was by no means fresh.

Temperature 99⁸, pulse 102, rate 26, blood pressure 98-52.

Physical Examination—Eye grounds pale and oedematous; moderate swelling of optic papillae.

Mouth—Abundant easily-bleeding labial herpes, tongue beef-red, stiff, oedematous and exhibiting slight atrophy of papilla; soft-palate and fauces oedematous and red, the swelling extending down to and involving the larynx and making swallowing and speech difficult. The gums were swollen, infected and two lower incisor teeth were loose; no pigment deposits.

Neck—Negative but for moderate adenopathy of posterior cervical chains.

Thorax—Mild oedema in both lung bases. *Heart* sounds soft and distant but no organic lesion.

Abdomen—Except for evidence of marked flesh loss and splashing sounds over stomach, negative.

Pelvis—(through rectum)—normal. The anus exhibited considerable congestion and the rectal mucosa was red and swollen but negative otherwise.

The Skin—Pale but dehydrated without pigmentation, ecchymoses, bruises or eruptions. Two small, shallow, ovoid bed sores, each about

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2 cm. in longest diameter, were seen over the ischial tuberosities.

Nervous System—To slight touch, hands and feet exquisitely tender but patient could shake hands without great discomfort and could stand on feet. The periarticular tissues were swollen but there was no fluid in any joint capsule. While the plantar reflexes were very brisk as were the knee jerks, there were no abnormal responses. No Kernig sign. Along the sciatic, obturator and intercostal nerves even mild pressure caused much pain. There were neither hand or wrist drops. Mentally the patient seemed more sulky than confused: certainly she was well oriented. Above, we have mentioned how, despite evident physical weakness and mental lassitude, the patient's expression was mobile and if one could judge by the eyes, cerebration was normal, even active.

Stomach Lavage—Slightly blood-stained due to mouth and throat congestion. About three pints of grass-green fluid containing much mucus and numerous milk curds were obtained. The odor was rather "musty", but not sickening. Free HCl was 6—total acidity 18. Bacterial study, roughly, was negative; Benzidin blood test +.

Stool—Only scant specimen seen; it was pale, watery and moderately rich with mucus and food flocculi. Benzidin test +.

Blood—Red blood count, 3,920,000; white count, 12,600; hemoglobin 60 (Tallquist); no smears studied.

Urine—Trace of albumin; occasional granular cast; negative for blood-derived pigment (see below).

SUMMARY

An advanced grade of malnutrition accompanied by anemia and evidences of some toxic or "deficiency" disturbance resulting in pernicious vomiting, diarrhoea, anemia, mucosal lesions in mouth and throat, neuritis, peripheral hyperaesthesia, joint swellings. Certainly, the physical examination and such bedside specimen analyses as I was able to carry out did not disclose the etiologic toxic cause and, from the patient's previous history of the abundant, diversified feeding commonly possible at a German farm-home (even a stingy German does not starve himself or his family!), no dietary deficiency seemed possible.

COMMENT

Diagnostically, even though the evidences of real disability amply were exhibited, to me the problem was a puzzling one. Search as I may, there was no organ or group of organs to which I could lay any primary dysfunction as being responsible for so rapid a physical decline in a young lady who, within four months, had been a physical specimen to be envied. Psychically, I could not exclude hysteria but felt that some factors other than hysteria and its effects required consideration or exclusion.

Possibly, as I sat and turned over in my mind the facts brought out by history and examination, I conveyed the impression to Dr. H. and the girl's parents that I was "stumped"; they left the room obviously not wholly satisfied. When they did so, I walked to the window and looked out upon the depressing environment: a slushy barnyard, dotted with numerous buildings, a group of bedraggled chickens were pecking about and a dozen cows sloshing aimlessly in a foot of January, Michigan mud.

Such outlook brought little inspiration and I was about to turn and question the patient further when a shadow to the left crossed my field of vision. Then it was that I became aware of a large, old-fashioned bureau topped by a huge mirror. And in the mirror a great part of the room was reflected, including the patient in her bed. Without changing my position and still apparently gazing into the barnyard, with my back to the sick girl, I saw her lean to her left as though to vomit in the vessel at the bedside. She regurgitated a small amount of fluid and accompanied it with a resonant belch. But, as I watched, interested at the apparent ease with which the girl moved about, I saw her direct a quick glance my way, then, seemingly satisfied that I was still enamored of the cows, her arm stretched out around the head-post of the huge wood bed and her hand secured something which, quickly, she transferred to her mouth. She chewed it slowly as I remained apparently oblivious to her acts and after a few minutes swallowed. I lingered a while at the window before I turned away. When I did so the girl was quiet and apparently dozing.

Without arousing her, I called to Dr. H. He entered, accompanied by the patient's mother. I asked the Doctor to assist me in moving the bed from the wall—a position which seemingly it had occupied for a long time. At once the girl sat up in bed and began to cry, moan and even curse—much to the astonishment of her mother and the Doctor. When the bed was moved from the wall, it was seen that the thick, dusty, dark green wall-paper had been torn in bits from the base-board upward for about two feet and inward from the left bed leg, a matter of eighteen inches.

My diagnosis of the persistent nervous "functional vomiting" and its effects now was clear. Dr. H. and I again passed the stomach tube into the now struggling, hysterically crying girl. Fragments of partly chewed wall-paper were secured, together with a few ounces of pale green fluid. Upon rubbing the thick, old wall-paper, a greenish dust stained my hand; by scraping, I secured about a half gram of similar powder, which specimen together with portions of the first and second gastric lavages, I took away for laboratory analysis. One did not have to await the very definitely positive Marsh tests for arsenic, returned from all the materials analyzed, to render a diagnosis of *chronic arsenical poisoning, self-induced.*

Aftermath—This hysterical young lady confessed, with much sobbing, that when her ambitions towards becoming a school teacher had been thwarted by her parents' refusal to allow her to complete the course at the normal school, she had decided to commit suicide. At simple lectures in chemistry there had been mentioned the many ways in which arsenic was used in the trades and the arts; among such was the common employment of

the metal in fabrics and wall-paper colorings. The "back-parlor" paper afforded an opportunity to test the effects of the drug: the patient became violently ill and really lost her nerve for any acute experiment. However, when ill, she found that she was treated kindly, was relieved of the constant work about the home and, what was, perhaps, the most comforting feature, escaped the mention of, and the courtship from, the parent-selected suitor. The scheme "worked": its carrying out greatly was facilitated when, for the convenience in nursing afforded by transforming the "back-parlor" into a bedroom, securing bits of green wall-paper sufficient to prolong the vomiting no longer became a problem. Eventually, the effects of the arsenic became so markedly incapacitating and the patient's dread of discovery (or recovery?) so great that the confused, distracted girl actually deemed it best that she continue her course until death occurred. Not a little support to the girl's determination was derived from the fear of her parents' anger should they ever learn the cause of her illness and from dread at the prospects of being compelled to marry the neighbor's son should she recover!

Suffice it to say, that after a frank discussion of matters with the girl and an interview with her parents, where the very "fear of God" over their heartlessness and its consequences was instilled into them, the situation was adjusted.

Careful nursing, feeding, sedatives, local applications to the joints, small doses of sodium thiosulphate and much psychotherapy resulted in rapid improvement. By mid-April, the patient was well physically and mentally and, from reports, again was "interested" in the young Irishman.

Certainly, this instance of "functional vomiting" deserves recording, if for nothing more than the mention of the happy accident which made the real diagnosis possible, when it seemed that one could say little more than "hysteria".

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CONTENTS

	Page
SECTION I—CLINICAL MEDICINE	
GASTRO-INTESTINAL STUDIES—V. GASTRIC JUICE IN ANEMIAS OTHER THAN PERNICIOUS ANEMIA—*Paul J. Fouls, M.D., O.M. Helmer, Ph.D., and L. G. Zerfas, M.D.*	667
THE INFLUENCE OF MUCILAGINOUS SUBSTANCES ON THE EMPTYING OF THE STOMACH—*H. Necheles, M.D. Ph.D., H. I. Sapoznik, M.D. R. Arens, M.D., and Jacob Meyer, M.D.*	684
STUDIES ON THE GASTRIC HUNGER MECHANISM—*Ira A. Manville, M.D. and Eldon G. Chuinard, Ph.D.*	688
CARCINOMA OF THE COLON—*Charles W. Heald, M.D.*	693
NOTES ON DIAGNOSIS AND PROGNOSIS IN GASTRIC ULCER: A CLINICAL STUDY OF FIVE HUNDRED CONSECUTIVE, OPERATIVELY DEMONSTRATED CASES—*Frank Smithies, Sc.D., M.D.*	697
AN UNUSUAL RIGHT DIAPHRAGMATIC HERNIA—*William C. Boeck, Ph.D., M.D., F.A.C.P. and Wells C. Cook, M.D.*	705
ABSTRACTS	707
DIVERTICULA OF THE JEJUNUM—*Jerome S. Levy, M.D. and A. De Groat, M.D.*	708
"OKRIN" AS AN ADJUVANT IN THE TREATMENT OF PEPTIC ULCER—*Arthur J. Atkinson, M.D.*	713
SECTION II—EXPERIMENTAL PHYSIOLOGY	
THE "CHEMICAL" PHASE OF GASTRIC SECRETION AND ITS REGULATION—*B. P. Babkin, M.D., D.Sc., F.R.S.C.*	715
ACCESSIBLE CLOSED LOOPS OF THE SMALL INTESTINE AND THE COLON—*G. E. Burget, Ph.D.*	722
THE BACTERIOCIDAL POWER OF THE STOMACH AND SOME FACTORS WHICH INFLUENCE IT—*Arthur Hanszen, M.S.*	725
SECTION III—NUTRITION	
A CONVENIENT METHOD OF ESTABLISHING DIET AND INSULIN THERAPY IN DIABETES—*Sister Mary Edwina, O.S.F., R.N.*	728
STUDIES IN FOOD ALLERGY—A PRELIMINARY REPORT—*Anton W. Oelgoetz, M.D., Paul A. Oelgoetz, B. A., and Juanita Willekind, R.N.*	730
ABSTRACTS	737
SECTION IV—ROENTGENOLOGY	
ROENTGENOGRAPHIC DIFFERENTIATION BETWEEN DIVERTICULITIS AND CANCER OF THE SIGMOID—*William H. Stewart, M.D., and H. Earl Illick, M.D.*	738
SECTION VIII—EDITORIAL	
ELECTRO-CHEMICAL PROCESSES UNDERLYING GASTRIC AND PANCREATIC SECRETION—*Walter C. Alvarez, M.D.*	743
SECTION IX—BOOK REVIEWS	
DIE PATHOLOGISCH-ANATOMISCHEN GRUNDLAGEN DER CHIRURGIE DES REKTUMKARZINOMS—*Dr. Heinrich Westhues, (Germany)*	745
SECTION X—AFTER "HOURS"	
ACADEMICIAN I. P. PAVLOV—*W. N. Boldyreff, M.D.*	747
SECTION XII—"THE CLINIC"	
POLYPOSIS OF DUODENUM AND JEJUNUM—REPORT OF AN INSTANCE—*John M. Cassidy, B.S., M.D. and Benjamin J. Macchia, M.D.*	755

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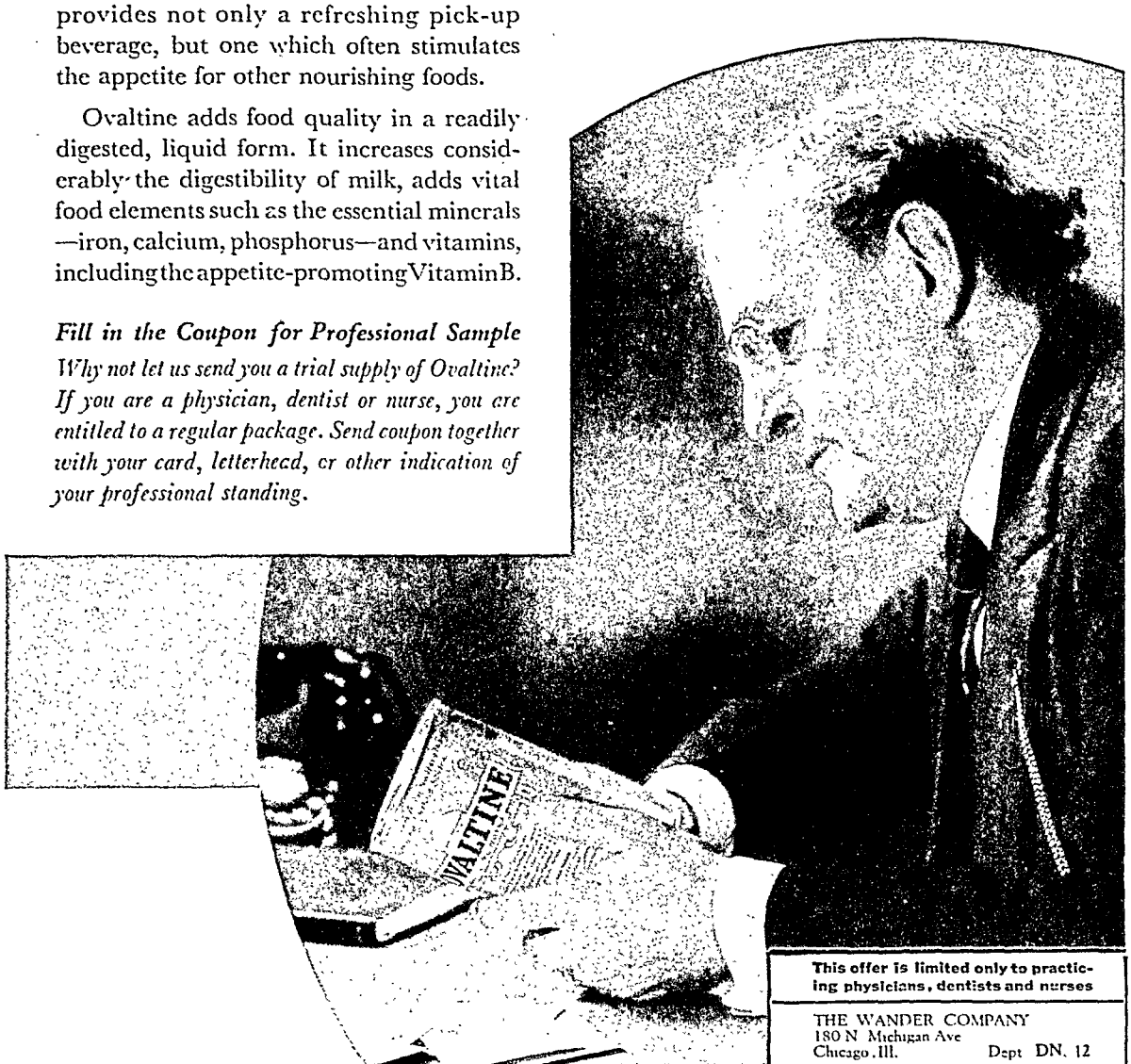
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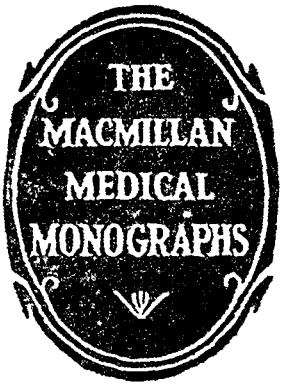
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A New 3-Way Attack On the Toxic Bowel

TOXIC BOWEL

1 Bacterial Hypersensitivity

2 Putrefaction
Flatulence

3 Intestinal Toxemia
So-called autointoxication
All conditions due to abnormal absorption from the bowel

4 Allergic and Atopic Conditions
Food Allergy
Urticaria
Eczema
Irritable Colon
Allergic Diarrhea, etc.

5 Colitis
Spastic
Mucous
Ulcerative

6 Intestinal Infections
Dysentery
Typhoid Fever
Asiatic Cholera

KARICIN

SORICIN*	KAOLIN
1 Desensitizes Decreases bacterial hypersensitivity and food allergy	**4 Adsorbs** Bacteria, Toxins, Toxic split proteins
2 Inhibits Proteolysis Decreases putrefaction and toxic absorption	**5 Soothes** Protects irritated intestinal mucosa
3 Detoxifies Bacteria and their toxins, Bacterial autolysates, Toxic products of putrefaction	**6 Modifies Bacterial Flora** Decreases proteolytic bacteria, Increases aciduric bacteria

* *Produced in nascent form from insoluble ricinoleate present in Karicin*

A NORMAL BOWEL

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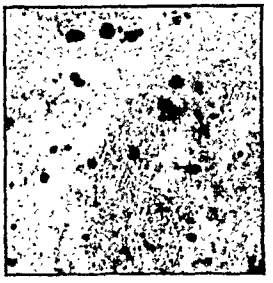
SCIENTIST'S CAMERA DISCLOSES VITAL DIFFERENCE IN BABY FOODS



Home-strained vegetables



Ordinary commercial-strained vegetables



Libby's Homogenized *Vegetables*

These are photomicrographs, picturing home-strained vegetables, ordinary commercial-strained vegetables, and Libby's *Homogenized* Vegetables magnified 100 times. Dark areas are food cells and fibers; note the differences in them. Since coarse fibers and tough-walled food cells are frequent causes of digestive upsets, it is easy to understand the greater safety of Libby's *Homogenized* Vegetables. Homogenization has the same dramatic and important effect on cereal, fruits, and soup.

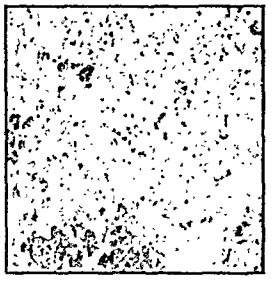
DIGESTION FAR MORE RAPID AND COMPLETE; BETTER NUTRITION SECURED



Home-strained vegetables after two hours of digestion



Ordinary commercial-strained vegetables after two hours of digestion



Libby's Homogenized *Vegetables after thirty minutes of digestion!*

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Libby's Homogenized FOODS FOR BABIES

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Gastro-Intestinal Studies*

V. Gastric Juice in Anemias Other Than Pernicious Anemia

By

PAUL J. FOUTS, M.D., O. M. HELMER, Ph.D.

and

L. G. ZERFAS, M.D.

INDIANAPOLIS, INDIANA

PREVIOUSLY[1] we reported the findings in the gastric contents, after histamine stimulation, of 47 patients having pernicious anemia and of normal subjects. Sixty-four additional patients typical of pernicious anemia have since been examined and each has exhibited a true anacidity. The term anacidity as used by us was defined[2] as "the condition in which there is an absence of titratable acid, pepsin, and rennin in the gastric contents after histamine stimulation".

It is the purpose of this paper to report the findings in the gastric juice after histamine stimulation of patients having anemias other than pernicious anemia.

MATERIALS AND METHODS

The methods used in collecting the gastric juice and for the determination of the pH, pepsin, and rennin were identical with those used in the previous report.[1] The pepsin is expressed in milligrams of 1:4000 U. S. P. pepsin and the rennin as milligrams of U. S. P. rennin. Samples which showed less than 0.1 mg. of rennin per cubic centimeter were recorded as containing no rennin. The titratable acid was determined either by Sahli's method or by titrating to neutrality, using phenol red as the indicator, as described previously.[2] The value thus obtained was expressed as the titratable acid rather than as the free acid. The total acid was determined by the customary method, but to conserve space only the titratable acid has been recorded in the tables.

In order to take into consideration the volumes of the individual samples of gastric juice as well as the concentrations of the acid and enzymes in the samples, the total amounts of acid and enzymes secreted during the first 60 minutes following the injection of histamine were determined and recorded in the tables. It was felt that this total gastric secretion would be a better index of gastric function than would the highest concentration of the acid and enzymes in the samples. Recently, Polland[3] has re-emphasized this fact.

RESULTS

Normals: Seventeen young, healthy individuals have now been examined by this method. Table I shows the findings in the gastric juice. The lowest pH values obtained during the tests varied between 1.0 and 1.2. The highest titratable acids varied between 80 and 140 c.c. of N/10 HCl per 100 c.c., with an average of 109 c.c. N/10 HCl per 100 c.c. The highest concentrations of pepsin ranged from 1.8 to 7.2 mg. per cubic centimeter, while the rennin varied between 17 and 70 mg. per cubic centimeter. The total amounts of titratable acid excreted during the 60 minutes varied between 66.9 and 223 c.c. N/10 HCl, averaging 122.1 c.c. The total amounts of pepsin varied between 268 and 956 mg., with an average of 525 mg. The rennin totaled from 2,335 to

TABLE I

Gastric Findings in 17 Young, Healthy Adults

Case No.	Lowest pH	Highest Titratable Acid c.c. N/10 per 100 c.c.	Highest Pepsin mg. per c.c.	Highest Rennin mg. per c.c.	Titratable Acid 60 Minute Secretion c.c. N/10	Pepsin 60 Minute Secretion mg.	Rennin 60 Minute Secretion mg.
1	1.0	109	1.8	17	155.2	275	2513
2	1.0	112	7.1	60	131.2	550	4626
3	1.0	98	4.3	60	96.2	391	4500
4	1.0	118	4.6	43	131.5	511	4912
5	1.0	133	7.2	70	155.3	956	7296
6	1.1	81	4.1	34	107.4	584	4798
7	1.0	140	5.4	68	221.8	750	9168
8	1.1	80	4.2	44	74.3	420	4437
9	1.0	104	2.3	19	102.3	268	2355
10	1.0	101	6.2	62	108.0	760	7505
11	1.2	85	4.3	52	66.9	382	4438
12	1.0	129	3.7	39	135.4	478	4890
13	1.1	107	5.2	52	72.9	470	4954
14	1.1	113	6.6	57	80.4	436	3811
15	1.0	100	3.7	45	100.0	408	4825
16	1.0	113	5.6	66	114.3	601	6832
17	1.0	126	4.1	58	223.0	681	8658

*From the Lilly Laboratory for Clinical Research, Indianapolis City Hospital, and the Department of Medicine, Indiana University School of Medicine.
Submitted October 24, 1934.

9,168 mg., averaging 5,323 mg. Thus the variation in gastric secretion in normals is great, as has been pointed out by Polland and Bloomfield,[4] but the extremes in this small group give a good index by which to judge the gastric secretion of the patients studied. In addition, the gastric juice of 115 medical students used in other studies was tested at the height of secretion for titratable acid; none of these showed a true anacidity.

ANEMIA

The gastric juice of 110 patients having varying grades of anemia was examined. Sixty-seven per cent of these patients had acid secretion values below the lower limits of the normals, while 56 per cent had enzyme values below the limits of the normals. The average titratable acid secreted for 60 minutes was 51.8 c.c. and the pepsin 273 mg. The decrease in acid was, therefore, proportionately greater than was the decrease in enzymes. Unless the decrease in acid was great there was usually little or no decrease in enzymes.

In Table II the patients are divided into groups as to degree of anemia, general condition and age. Examination of this table shows that the patients having the more severe grades of anemia are more apt to have decreased gastric secretion. This is shown both by the percentages of the groups having acid and enzyme secretion below the lower limits of normal and by the average secretions of titratable acid and pepsin of the groups. However, the general condition of the patient, as was demonstrated by Bloomfield and Keefer,[5] has even more influence on the gastric secretion than has

TABLE II

Gastric Findings of the Patients Grouped According to Degree of Anemia, General Condition and Age

	Hemoglobin (Newcomer)			Condition of Patient			Age	
	60% up	40-60%	0-40%	Good	Fair	Poor	40-80	8-40
Number of cases	45	38	25	30	33	37	60	48
Per cent of anacidities	13	18	20	23	15	11	17	17
Per cent of patients with titratable acid below 66.9 c.c.	55	71	80	46	76	81	73	58
Per cent of patients with pepsin below 268 mg.	47	56	72	36	61	70	63	46
Average titratable acid (c.c.)	60.9	47.6	41.7	65.3	54.7	35.5	49	56
Average pepsin (mg.)	318	264	205	332	271	203	249	302

the degree of anemia. The high percentage of anacidities in the group considered to have good general condition can be accounted for by the fact that most of the patients having idiopathic hypochromic anemia are included in this group. As was to be expected, the age of the patient apparently influenced the gastric secretion. There was very little difference in the 10-year periods between 40 and 80, although the percentage of patients in the age-group above 40 having decreased acid and enzymes was much greater than in the age-group below 40. The percentage of patients having anacidity was identical in the two age-groups.

It was felt that the findings in this paper show that true anacidity is a permanent condition and that, therefore, the degree of anemia, general condition of the patient and age of the patient cannot influence the condition of the gastric secretion in patients having true anacidity. Therefore, Table III was prepared to show the findings

TABLE III

Gastric Findings of the Patients Not Having Anacidity Grouped According to Degree of Anemia, General Condition and Age

	Hemoglobin (Newcomer)			Condition of Patient			Age	
	60% up	40-60%	0-40%	Good	Fair	Poor	40-80	8-40
Number of cases	39	31	20	30	28	33	50	40
Per cent of patients with titratable acid below 66.9 c.c.	48	64	75	30	71	79	66	50
Per cent of patients with pepsin below 268 mg.	38	45	65	13	54	67	56	35
Average titratable acid (c.c.)	70.3	58.4	52.1	84.9	64.5	39.3	58.8	67.3
Average pepsin (mg.)	367	324	256	432	330	228	298	363

in the group of cases not having true anacidity. The findings are similar to those in Table II except as to the general conditions of the patients. The influence of the general condition of the patient on the gastric secretion is much more apparent in Table III.

The above generalizations, of course, do not apply to each individual case. For instance, the patient having the highest acid value was 65 years of age, was in very poor general condition and had a hemoglobin of 30 per cent.

The examination of the subsequent tables demonstrates the value of determining the total secretion over a 60-minute period. Several of the patients had approximately normal concentrations of acid and enzymes in the gastric juice, but when the volumes of the samples are considered, the gastric secretion is shown to be decreased definitely.

The patients were divided into groups according to their clinical diagnoses. Each group now will be considered separately.

I. *Idiopathic Hypochromic Anemia:* Seventeen patients, three males and 14 females, were typical, clinically and hematologically, of idiopathic hypochromic anemia. The gastric findings and the blood counts of the patients are recorded in Table IV. All of the patients exhibited decreased acid and enzyme values when the anemia was present. Ten of them had true anacidity. Thus this group contained 55 per cent of the patients having anacidity, although the group made up only 15 per cent of the complete series of patients. In four of the patients with anacidity the gastric contents were re-examined after the blood had returned to normal or near-normal values and in each the anacidity was still present. Hartfall and Witts[6] reported the persistence of gastric deficiency in a number of similar cases which were re-examined after as many as seven years.

TABLE IV

Blood and Gastric Findings in Patients Having Idiopathic Hypochromic Anemia

Case No.	Age	Date	Red Blood Cells millions per cu. mm.	Hemoglobin % (Newcomer)	Lowest pH	Highest Titratable Acid c.c. N/10 per 100 c.c.	Highest Pepsin mg. per c.c.	Highest Rennin mg. per c.c.	Titratable Acid 60 Minute Secretion c.c. N/10	Pepsin 60 Minute Secretion mg.	Rennin 60 Minute Secretion mg.
1	57	9-27-32	4.30	83	8.0	0	0	0	0	0	0
2	37	5- 2-32	4.60	67	7.0	0	0	0	0	0	0
	38	6-23-33	3.88	51	7.7	0	0	0	0	0	0
3	50	5- 2-33	4.32	33	8.1	0	0	0	0	0	0
4	38	2- 7-33	4.40	44	7.4	0	0	0	0	0	0
5	35	2- 9-32	2.85	33	8.2	0	0	0	0	0	0
	36	1-14-33	5.17	79	8.2	0	0	0	0	0	0
6	48	3-25-32	3.33	36	7.6	0	0	0	0	0	0
7	25	2-12-32	5.90	86	8.2	0	0	0	0	0	0
	25	12-12-32	5.26	68	8.0	0	0	0	0	0	0
	27	5- 7-34	5.06	85	7.6	0	0	0	0	0	0
8	41	2-24-32	6.55	96	7.0	0	0	0	0	0	0
		12-12-32	5.07	72	7.0	0	0	0	0	0	0
9	21	10- 2-33	5.26	53	6.9	4	1.2	4	0.4	11	36
10	63	6-12-33	4.64	42	1.7	36	1.9	19	15.8	76	599
11	28	7-27-33	4.24	33	2.1	33	1.0	10	8.0	19	227
		11- 1-33	5.58	84	2.2	21	0.3	2	6.8	14	
12	65	2-25-33	4.54	51	1.3	78	3.2	33	6.2	26	264
		11- 7-33	4.82	92	1.0	121	4.0	43	103.4	346	3615
13	..	5-27-33	4.51	69	2.1	22	3.0	33	18.9	291	3372
14	65	8-26-33	1.56	16	3.5	19	2.7	41	1.6	27	318
		11-10-33	4.86	85	1.0	81	2.8	37	47.0	150	1865
15	56	8-18-33	2.99	37	1.2	63	2.8	24	36.5	176	1119
16	29	12-11-33	3.50	43	7.7	0	0	0	0	0	0
17	43	3-26-34	4.91	65	8.3	0	0	0	0	0	0

Case 8 is of special interest. He was first seen on September 12, 1928, at which time he had an achlorhydria (after an Ewald test meal) and a severe secondary anemia. He responded well to iron but it was found that he required iron daily to maintain a normal hemoglobin percentage. At the time (February 24, 1932) he had the first analysis following histamine stimulation he had a normal blood picture and was symptom-free. About seven months later he developed gastric distress, and gastro-intestinal X-rays on December 20, 1932, revealed a cancer of the pylorus. Exploratory laparotomy revealed an inoperable condition, and the patient died on June 2, 1933. Hurst[7] also reported a patient with simple achlorhydric anemia who later developed a carcinoma of the stomach.

Case 12 had no titratable acid in any samples up to the 60-minute sample. In that sample near-normal concentrations of acid and enzymes were found, although the volume of the sample was very small. After the blood had returned to normal, near-normal values for acid and enzyme secretion were obtained. Two other patients who had markedly decreased gastric function were re-examined after the blood had reached normal. One of these showed a marked improvement, while the other showed no improvement. The results in the few cases in which repeated gastric analyses were done would indicate that when there is true anacidity present the condition, as in pernicious anemia, is permanent. However, in those cases with small amounts of titratable acid (pH 3.5 to 7) the gastric function may or may not improve.

The incidence of anacidity in this group of patients having idiopathic hypochromic anemia is similar to that reported by Wintrobe and Beebe.[8] They divided their cases into four groups: namely, (1) no free acid after histamine (60 per

TABLE V

Blood Counts and Gastric Findings in Patients Having Anemia Due to Acute or Chronic Hemorrhage

Case No.	Age	Diagnosis	Date	Red Blood Cells millions per cu. mm.	Hemoglobin % (Newcomer)	Lowest pH	Highest Titratable Acid c.c. N/10 per 100 c.c.	Highest Pepsin mg. per c.c.	Highest Rennin mg. per c.c.	Titratable Acid 60 Minute Secretion c.c. N/10	Pepsin 60 Minute Secretion mg.	Rennin 60 Minute Secretion mg.
18	24	Bleeding gastric ulcer	11-16-33	4.32	52	1.0	100	4.2	45	68.1	280	2904
19	44	Hypertension, G. I. bleeding	10-14-32	5.73	59	1.3	57	3.1	28	57.4	267	2961
20	64	Gastric ulcer, Chronic hemorrhage	3-16-32	2.46	40	1.1	99	4.0	44	54.2	221	2534
21	65	Bleeding gastric ulcer	11- 6-33	2.36	30	1.0	121	3.3	34	256.3	639	6830
22	47	Bleeding duodenal ulcer	4-28-33	2.15	31	1.1	101	5.2	49	150.3	656	5993
23	50	Chronic hemorrhage G. I. tract	1-26-34	3.92	50	1.0	103	2.1	18	56.9	134	1146
24	38	Chronic hemorrhage, Hemorrhoids	4- 6-34	2.30	31	1.0	107	5.6	43	151.8	718	5370
25	25	Ulcerative colitis	1- 5-34	4.00	42	1.1	97	1.7	17	140.1	316	3230
26	60	Melena—unknown cause	9-30-32	3.32	52	1.0	116	8.8	79	136.4	1071	9046
27	31	Chronic hemorrhage, Hemorrhoids	2-16-32	2.64	27	1.2	67	2.5	23	72.7	370	2169
28	51	Hemorrhoids	8-29-32	3.17	49	1.0	112	2.9	41	153.3	389	4995
29	42	G. I. bleeding, Hemorrhoids	4-17-33	3.80	52	1.3	79	3.4	37	69.4	291	3008
30	21	G. I. bleeding	5- 3-33	4.73	78	1.2	72	3.6	38	101.6	606	5943
31	28	Menorrhagia	9-11-32	4.46	69	1.1	100	2.6	29	74.3	231	2436
32	43	Fibroids	7-12-32	2.45	28	1.0	98	4.7	..	55.5	233	
33	24	Miscarriage	3- 2-32	1.62	26	4.2	6	1.5	14	1.1	34	287
			3-23-32	3.12	49	1.9	20	2.4	19	4.6	76	578
34	31	Abortion	6- 3-32	2.62	41	1.1	63	4.0	35	48.6	277	2449
35	16	Abortion	6- 1-32	3.47	45	1.0	100	4.1	35	41.5	221	1744
36	38	Abortion	6- 1-32	3.20	45	1.2	61	5.2	43	49.4	418	3265
37	37	Post-partum hemorrhage	1-31-33	3.31	43	1.1	70	10.0	75	91.8	1135	8081

cent); (2) low or normal amounts of free HCl after histamine although the Ewald meal had been ineffective in eliciting acid (23 per cent); (3) hypochlorhydria (Ewald) (8.5 per cent); and (4) cases in which secretion of HCl seemed to be normal (8.5 per cent).

II. *Hemorrhage:* Of the 20 patients having anemia due to acute or chronic hemorrhage none had an anacidity (Table V). There were 13 patients who had hemorrhage from the gastro-intestinal tract. Six of these had higher acid values than the average of the normal and only three fell below the lowest normal. The average was 121.2 c.c. N/10 HCl—just below that of the normals. Only two of the group had enzyme values below the lowest normal, while the average (458 mg.) approximately was that of the normals. The seven remaining patients had anemia due to vaginal bleeding. The patient having *post-partum* hemorrhage had normal acid and very high enzyme values (1,134.6 mg. pepsin). All of the rest had slightly decreased acid values, although in only one were the enzyme values as markedly reduced as the acid.

This one patient (Case 33) should be included in the anemia of pregnancy group as well as in this group. She was first seen following a spontaneous abortion accompanied by a severe hemorrhage. The administration of iron was followed by a return of the blood to normal and an apparent increase in gastric function. The patient soon became pregnant again. The daily administration of iron kept the blood normal and the patient was delivered of a full-term infant. She then voluntarily discontinued the iron therapy. She received no iron during the next pregnancy and she aborted at the end of three months. She again entered the hospital after a severe hemorrhage, with a red blood cell count of 1.40 million and a hemoglobin of 34.2 per cent. Apparently this patient's gastric function becomes so poor during pregnancy that a severe anemia develops and the patient aborts unless iron is administered.

The decreased acid secretion in the three patients having anemia following abortions may have been in part due to the decrease occurring during pregnancy. Strauss and Castle[9] reported a decrease in gastric acidity during pregnancy and stated that anemia of pregnancy is found in only those patients who have had for some time defective diets or dietary deficiencies conditioned by gastric anacidity or related gastro-intestinal disturbances.

III. *Pellagra and Dietary Deficiency Anemias:* In Table VI are recorded the gastric findings in eight patients having pellagra with anemia and 16 other patients having dietary deficiencies with anemia. Six of the pellagrous patients had markedly decreased gastric secretion before treatment. Two of these had true anacidity, while Case 41 would have had an achlorhydria to Toepfer's reagent at the first examination. Case 45 had mild pellagra due to restricted food intake during the course of a chronic infectious arthritis, and there was no decrease in enzymes and only slight decrease in acid secretion. Case 38 had had a posterior gastro-enterostomy ten years previously. The other patient with anacidity (Case 42) still had the anacidity after the disappearance of all the symptoms of pellagra. Cases 39, 41 and 43 showed definite improvement of the gastric function after improvement of the pellagra and the anemia. Cases 41 and 42 again demonstrate that if there is a true anacidity after his-

TABLE VI

Blood and Gastric Findings in Patients Having Pellagra with Anemia and Nutritional Anemias

Case No.	Age	Diagnosis	Date	Red Blood Cells millions per cu. mm.	Hemoglobin % (Newcomer)	Lowest pH	Highest Titratable Acid c.c. N/10 per 100 c.c.	Highest Pepsin mg. per c.c.	Highest Rennin mg. per c.c.	Titratable Acid 60 Minute Secretion c.c. N/10	Pepsin 60 Minute Secretion mg.	Rennin 60 Minute Secretion mg.
38	51	Pellagra, Gastro-enterostomy	1-10-31	5.11	59	7.0	0	0	..	0	0	
39	18	Pellagra	4-28-33	3.32	65	1.9	26	5.1	52	12.0	228	2253
			6-30-33	4.33	78	1.2	112	3.3	35	145.1	469	4949
40	38	Pellagra	2-24-33	2.09	58	1.1	102	4.4	43	80.3	376	3734
41	50	Pellagra	6-28-33	4.55	75	6.3	7	2.2	24	3.8	127	1357
			7-21-33	5.23	78	2.7	18	1.7	19	5.9	65	696
42	30	Pellagra	6-28-33	3.47	57	8.6	0	0	0	0	0	0
			7-10-33	3.67	66	8.6	0	0	0	0	0	0
43	54	Pellagra	8- 3-34	3.45	75	2.1	30	..	19	2.6	...	167
			9- 5-34	4.55	101	2.3	22	..	15	9.3	...	580
44	46	Pellagra	8-24-34	4.06	67	..	49	..	48	40.9	...	4079
45	20	Pellagra, Atrophic arthritis	8-15-33	4.19	67	1.1	88	7.4	77	56.5	488	5346
46	33	Dietary anemia	1- 5-34	4.41	66	1.1	101	5.2	58	110.1	583	6519
47	30	Dietary anemia	1-17-33	4.55	71	1.3	58	2.9	39	54.6	310	3657
48	18	Dietary anemia	9-16-32	4.05	74	1.0	144	5.7	83	181.3	597	7666
49	29	Dietary anemia	1- 4-33	4.16	64	1.0	112	3.6	42	83.4	269	2950
50	17	Dietary anemia	10- 2-33	4.85	67	1.1	91	4.5	43	102.0	480	4472
51	26	Dietary anemia	3- 2-34	4.32	75	1.0	104	6.5	65	80.6	555	5206
52	31	Dietary anemia	11-10-33	5.00	78	1.0	108	5.1	63	67.5	283	3574
53	50	Dietary anemia	5-23-33	4.20	79	1.1	128	5.4	67	212.1	783	8712
54	52	Dietary anemia	8-25-33	4.50	76	1.8	37	4.8	39	10.1	137	1361
55	55	Dietary anemia	3-16-34	4.86	79	1.3	64	4.2	..	43.6	302	
56	33	Dietary anemia	10- 1-32	3.50	65	1.1	84	3.2	28	123.2	441	3802
57	40	Dietary anemia	2-22-33	4.66	73	1.7	52	1.2	9	10.2	31	241
107	26	Diarrhea	2-23-32	1.73	37	1.6	32	2.1	20	21.2	155	2071
108	53	Chronic diarrhea	2-19-32	4.63	93	1.1	105	3.6	..	92.9	346	
			10-31-33	5.40	83	1.1	98	2.6	26	136.7	406	4468
109	55	Macrocytic anemia	5- 7-32	3.86	83	1.7	34	5.2	45	8.1	244	
110	72	Chronic diarrhea, combined system disease	12-20-32	4.60	83	1.2	95	4.6	39	45.7	272	2400

TABLE VII

Blood and Gastric Findings in Patients Having Anemias Refractive to Medication

Case No.	Age	Diagnosis	Date	Red Blood Cells millions per cu. mm.	Hemoglobin % (Newcomer)	Lowest pH	Highest Titratable Acid c.c. N/10 per 100 c.c.	Highest Pepsin mg. per c.c.	Highest Rennin mg. per c.c.	Titratable Acid 60 Minute Secretion c.c. N/10	Pepsin 60 Minute Secretion mg.	Rennin 60 Minute Secretion mg.
58	55	Tabes dorsalis	12-28-32	4.42	76	1.0	103	4.5	47	223.0	796	8117
59	46	General paresis	11- 1-32	4.30	75	1.0	109	5.7	78	80.2	323	3364
60	52	Chronic cystitis, Chronic gastritis	8- 7-33	4.32	72	2.1	21	0.5	6	4.6	15	128
			8-31-33	...	..	6.3	2	0.8	2	0.7	23	74
61	50	Streptococcic septicemia	8-16-32	3.11	40	1.2	74	4.3	57	74.6	405	5307
62	54	Pansinusitis, Lues	2- 7-33	1.93	37	8.3	0	0	0	0	0	0
63	66	Infectious arthritis	8-13-34	4.20	69	4.0	10	..	38	1.4	...	564
64	35	Abscess—chest wall	8-13-34	3.38	43	1.0	119	..	88	114.4	...	8513
65	50	Chronic nephritis	2-24-32	1.14	25	1.2	70	2.6	24	80.1	357	
66	54	Chronic nephritis	6-12-33	3.49	49	1.2	92	5.0	49	18.3	96	912
67	60	Chronic nephritis	8-22-33	3.33	55	1.0	96	5.8	67	172.1	1013	12480
68	45	Hypertension	2-23-33	4.56	78	1.0	115	4.0	47	..	..	
69	76	Chronic nephritis	1-18-34	2.06	29	7.6	0	0	0	0	0	0
70	38	Chronic nephritis	2- 5-34	4.31	84	1.1	103	4.1	52	75.2	284	
71	50	Carcinoma of colon with metastases	4-21-33	4.33	47	1.7	36	2.6	24	19.9	141	1288
72	29	Myelogenous leukemia	2-15-32	3.50	57	1.4	56	2.4	37	49.4	257	3795
73	65	Myelogenous leukemia	7-21-33	1.15	24	4.9	14	2.5	34	2.4	63	710
74	58	Multiple myeloma	5-16-33	1.88	39	4.3	28	0.8	8	...	..	
75	60	General carcinomatosis	9-19-33	3.48	44	6.7	...	..	5	...	...	
76	57	General carcinomatosis	2-16-34	2.15	39	3.7	20	2.6	34	13.5	189	2378
77	35	Multiple sclerosis	2-17-33	4.37	44	1.4	45	3.0	30	82.1	700	7595
78	59	Carcinoma of stomach	2-16-32	1.81	17	1.0	93	6.2	61	62.3	507	
79	55	Carcinoma of stomach, Pellagra	5-29-33	3.20	58	8.0	0	0	0	0	0	0
80	53	Carcinoma of stomach	3-18-32	2.60	40	4.5		0.5	4		12	72
81	66	Carcinoma of stomach	5-23-33	4.81	75	1.2	110	5.2	72	78.0	486	7141
82	57	Carcinoma of stomach	11- 6-33	4.30	73	3.5	30	0.2	2	...	...	
			11- 8-33	...	..	3.7	32	0.2	..	19.7	13	
83	55	Carcinoma of stomach	5-29-34	2.29	56	1.7	48	..	12	5.9	...	190
8	41	Carcinoma of stomach, Hypochromic anemia	12-12-32	5.07	72	7.0	0	0	0	0	0	0
84	50	Carcinoma of stomach	1- 8-34	3.80	48	6.5	8	2.5	..		35	
85	32	Aplastic anemia	8-16-33	0.94	18	2.1	29	2.0	16	10.9	91	696
86	8	Cirrhosis of liver	3- 8-32	4.32	66	1.7	39	2.3	24	15.6	120	1220
87	44	Cirrhosis of liver	4- 9-34	3.37	67	1.3	64	3.7	35	59.8	238	2073
88	57	Macrocytic anemia	6- 9-33	1.83	39	2.0	27	4.5	47	14.0	204	2481

tamine the condition is permanent, whereas if there is a slight amount of acid titratable to pH 7 there may be an improvement in the gastric secretion. It seems probable that the patients with pellagra reported in the literature as having a return of free acid are similar to Case 41 rather than to the patients having true anacidity.

Of the 12 patients having deficiency anemias, eight had gastric function within normal limits, while only two had very small amounts of acid and enzymes. The remaining two had slightly decreased acid and normal enzyme values. Only three of Mettier and Minot's[10] nine cases of anemia due to deficient diet, had normal acid findings. However, their patients had severer anemias than most of the patients in this group.

Four patients had anemia which could not be differentiated from that seen in primary pernicious anemia. All of these responded to liver extract, although Cases 107 and 108 require parenteral liver extract to maintain normal red blood cell counts. These patients have conditioned deficiencies which apparently were produced by the failure of absorption from the gastro-intestinal tract. In all but one there was a decrease in acid and, to a less extent, enzymes. Case 108, who had a normal gastric analysis after histamine, three years previously had had an achlorhydria to an Ewald test meal. However, three months later, after his blood had returned to normal, another Ewald test meal revealed the presence of free HCl. At the present time this patient, although he has apparently a normal gastric secretion, requires liver extract by injection to maintain a normal red blood count. Case 110 at the time of examination of the gastric contents had a normal red blood count, but he had previously had an anemia which responded to liver extract and he still had definite signs of combined system disease. Cases 107, 108 and 110 have had chronic diarrheas of many years' duration, with the resulting faulty absorption which factor probably was of etiological importance in the production of the anemia.

IV. *Anemias Refractive to Medication:* This group of patients (Table VII) had anemias responding poorly or not at all to medication. In eight patients the anemia apparently was due to infection. The titratable acid was below the average of the normals in all but two of these patients, but in only three was it below the lower limits of normal. Case 62 was the only one having a true anacidity. This patient had a blood picture similar to that seen in pernicious anemia. There was a marked, chronic pansinusitis in addition to tertiary lues. His blood did not respond to large doses of iron and Liver Extract No. 343 administered by mouth or to daily doses of liver extract (that derived from 100 gm. of liver) administered parenterally. The markedly decreased gastric secretion in Case 60 might have been accounted for by the chronic gastritis which was present. These findings in the few patients with infection do not entirely agree with those of Chang[11] who reported a decrease in gastric acidity to one-third of normal in febrile conditions and stated that anemia and general fitness played no important role in this decrease.

TABLE VIII

Blood Counts and Gastric Juice Findings in Patients Having Primary Endocrine Disturbances

Case No.	Age	Diagnosis	Date	Red Blood Cells millions per cu. mm.	Hemoglobin % (Newcomer)	Lowest pH	Highest Titratable Acid c.c. N/10 per 100 c.c.	Highest Pepsin mg. per c.c.	Highest Rennin mg. per c.c.	Titratable Acid 60 Minute Secretion c.c. N/10	Pepsin 60 Minute Secretion mg.	Rennin 60 Minute Secretion mg.
89	60	Acromegaly	1- 4-33	4.35	72	8.0	0	0	0	0	0	0
90	22	Simmonds' disease	10-10-33	2.99	72	1.1	83	4.1	45	60.7	253	2609
91	41	Ovarian dyscrasia	12-28-32	4.78	78	1.2	66	3.8	46	81.6	503	5756
92	61	Myxedema	11- 7-32	3.90	74	1.3	37	2.3	22	31.9	238	2394
93	70	Myxedema	2- 6-33	3.37	68	1.0	116	10.0	62	182.2	1146	6560
94	28	Myxedema	4-23-34	4.24	84	7.2	0	0	0	0	0	0
95	30	Myxedema	7-12-34	2.96	59	7.0	0	0	0	0	...	0
			8-16-34	3.04	57	8.2	0	0	0	0	...	0

Of the six patients having anemia associated with nephritis two had normal acid and enzyme values, while in the others the gastric secretion definitely was decreased, although in only one, age 76, was there an anacidity. The severity of the nephritis had no apparent relationship to the gastric secretion. Case 8, who had very severe nephritis with nitrogenous retention, had a higher total pepsin value than any of the normals.

Six patients had either generalized carcinomatosis or leukemia and all of these had markedly decreased acid and enzyme values. The general condition of each of these patients was poor. Although none had a true anacidity, four would have been considered so if Toepfer's reagent had been used as the indicator. Eight patients examined had carcinoma of the stomach with secondary anemia. Two of these had true anacidity and three additional patients had such small amounts of acid that no free acid would have been recorded if Toepfer's reagent had been used as the indicator. Another patient had small amounts of acid and enzymes, while the two remaining patients had near normal acid and enzyme secretion. Of the two cases with true anacidity, one had pellagra secondary to the carcinoma and the nephritis with nitrogenous retention, had a higher total pepsin value than any of the normals.

Achlorhydria recently has been reported in carcinoma of the stomach in from 50 to 90 per cent of the cases. This is in contrast to the previously held view that the presence of free acid in the stomach contents contraindicated a diagnosis of malignancy. It would seem from our few cases that even a greater per cent of patients would show titratable acid if the gastric contents were titrated to pH 7 rather than to an end-point of 3.5. However, Hurst[12] maintained that achlorhydria is the result of a chronic gastritis which precedes the onset of carcinoma and is the commonest predisposing condition. He, therefore, divided gastric cancer into two groups: a primary, following chronic gastritis, and a secondary, following a chronic simple ulceration. Nevertheless, it would seem that this method of determining the titratable acid to pH 7 and the determination of the enzymes would be of great aid in many cases in the differential diagnosis between cancer of the stomach and pernicious anemia.

Each of the two patients having cirrhosis of the liver with a microcytic type of anemia had decreased acid secretion. One patient with aplastic anemia had markedly decreased acid and enzyme secretion. Case 88 had a macrocytic anemia, the cause of which could not be ascertained, and had greatly reduced acid secretion although the enzymes were not so greatly lacking. This patient did not respond to liver extract or iron administered by mouth or to liver extract given parenterally.

It would, therefore, seem that, in this group, the failure of response to medication was a result of the primary condition rather than of a failure of gastric secretion, as all degrees of gastric secretion may be found in the group.

V. *Anemia Associated with Endocrine Dysfunction:* In Table VIII are recorded the gastric findings of seven patients having primary endocrine dysfunctions associated with anemia. Of

TABLE IX

Gastric Juice Findings and Blood Counts of Patients Having Anemia of Pregnancy

Case No.	Age	Diagnosis	Date	Red Blood Cells millions per cu. mm.	Hemoglobin % (Newcomer)	Lowest pH	Highest Titratable Acid c.c. N/10 per 100 c.c.	Highest Pepsin mg. per c.c.	Highest Rennin mg. per c.c.	Titratable Acid 60 Minute Secretion c.c. N/10	Pepsin 60 Minute Secretion mg.	Rennin 60 Minute Secretion mg.
96	31	Anemia of pregnancy	7-24-33	4.23	47	1.3	73	3.8	39	60.2	317	3124
97	30	Anemia of pregnancy with polyneuritis	5- 4-33	3.58	56	1.3	75	4.3	41	33.8	313	2546
98	30	Anemia of pregnancy	8- 8-33	3.20	55	1.8	37	4.0	49	43.4	498	5909
99	26	Anemia of pregnancy	3-14-34	4.67	79	1.0	100	4.6	38	82.4	567	4589
100	36	Anemia of pregnancy	4-13-34	3.63	54	6.8	3	..	2	0.7	...	61
101	25	Anemia of pregnancy	9- 4-34	5.12	97	4.0	12	..	7	2.3	...	140
			9-14-34	3.59	34	1.3	82	..	49	55.7	...	3146

TABLE X

Blood Findings and Gastric Analyses of Patients Having Hemolytic Anemia

Case No.	Age	Diagnosis	Date	Red Blood Cells millions per cu. mm.	Hemoglobin % (Newcomer)	Lowest pH	Highest Titratable Acid c.c. N/10 per 100 c.c.	Highest Pepsin mg. per c.c.	Highest Rennin mg. per c.c.	Titratable Acid 60 Minute Secretion c.c. N/10	Pepsin 60 Minute Secretion mg.	Rennin 60 Minute Secretion mg.
102	56	Hemolytic jaundice	6-27-32	3.94	56	1.0	132	7.1	87	144.6	575	7842
103	20	Hemolytic jaundice	4-26-32	2.87	61	1.0	106	4.8	40	129.4	535	3820
104	10	Hemolytic jaundice	3- 1-32	2.24	..	1.6	42	2.1	57	55.2	254	5050
105	48	Hemolytic anemia	5-20-33	1.85	36	1.5	64	5.9	57	16.3	193	1973
106	74	Hemolytic anemia	8-18-34	1.60	38	1.2	66	..	48	29.5	...	1711

the four patients having myxedema, two had true anacidity, one a markedly decreased function, and the fourth had high total amounts of both acid and enzymes. Lerman and Means,[18] using histamine as a gastric stimulant, found that nine out of 17 patients with myxedema had achlorhydria, and stated that anemia was more frequent among the patients having achlorhydria. Case 89, who had acromegaly, showed an anacidity, while Case 90, who had Simmonds' disease (Cachexia Hypophyseopriva), had acid and enzyme values within the lower limits of normal. Silver[14] reported the common occurrence of achlorhydria in cases of Simmonds' disease. His patient had achlorhydria after histamine stimulation, although he states that ferments were present. The one patient having ovarian dyscrasia had normal acid and enzymes in the gastric juice.

VI. *Anemia of Pregnancy.* Six patients having anemia associated with pregnancy were examined (Table IX). All had decreased acid values, although in only one was the enzyme secretion definitely decreased. This patient had a second examination five months after delivery. There had been a definite but slight improvement in secretion although there still was not enough acid to be recorded using Toepfer's reagent as the indicator. Case 33, who was included in Group II, should be included in this group also. This patient likewise had markedly decreased acid and enzyme values.

These few cases indicate that the decrease in acid usually precedes the decrease in enzymes during pregnancy.

VII. *Hemolytic Anemias:* Three patients having hemolytic jaundice were examined. The two adults (Table X) had normal gastric secretion, while the boy, age 10, had slightly decreased acid secretion. The two patients having severe hemolytic anemia (cause unknown) had markedly decreased gastric secretion although neither had an anacidity.

SUMMARY AND CONCLUSIONS

The examination of the gastric contents, in this series of patients having anemias other than pernicious anemia, demonstrates that a majority of the patients have decreased gastric secretion. The degree of anemia seemed to have some influence on this decrease, as the patients with the more severe degrees of anemia were more apt to have decreased gastric function, although this was by no means always the case. The only group consistently having a marked decrease in gastric secretion was that of the idiopathic hypochromic anemias. Each patient of this group had very physiologically inadequate gastric secretion to the test meal employed at the time of the anemia, and 10 of the 18 patients in the series who had true anacidity belonged to this group. The patients having anemia of pregnancy and those having anemia following abortions or miscarriages also had decreased acid secretion, but this was usually not so pronounced as it was in the idiopathic, hypochromic anemia group. The incidence of decreased gastric secretion also was especially high in patients having pellagra, carcinoma of the stomach and in those patients having very poor general physical condition. There was no constant finding in the gastric contents of the patients not responding to medication.

Previously,[2] it was demonstrated that no enzymes can be found in gastric juice having pH of 7 or above. This series shows that titrating the gastric juice to pH 7 may be of value in differential diagnosis and in prognosis as to the possible improvement of the gastric secretion. Each of 111 patients typical of pernicious anemia had a pH of 7 or above and exhibited no enzymes in the gastric contents, yet only two of eight patients having carcinoma of the stomach had similar findings. Therefore, the use of this technique may be of great aid in the differential diagnosis between pernicious anemia and carcinoma of the stomach.

We were not able to demonstrate a return of gastric secretion in patients whose gastric contents after histamine stimulation had pH values above 7 and no gastric ferments. However, there was definite improvement in the gastric secretion in four patients whose gastric contents had pH values between 3.5 and 7 (no free HCl to Toepfer's reagent) when first examined. Therefore, it would seem that, if a true anacidity is present, the condition is permanent, but that an improvement is possible if a small amount of titratable acid is present in the gastric juice.

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The Influence of Mucilaginous Substances on the Emptying of the Stomach*

By

H. NECHELES, M.D., Ph.D.; H. I. SAPOZNIK, M.D.;
R. ARENS, M.D., and JACOB MEYER, M.D.
CHICAGO, ILLINOIS

JONES, Ivy and Atkinson (1) reported on the *favorable action of okrin*, the mucilaginous substance of okra, in the treatment of peptic ulcer. We (2) studied the effect of the dried, dehydrated powdered okra pods on peptic ulcer and on the secretion of the stomach. The study already published showed an improvement in a number of ulcer patients and an increase in the acidity of the resting stomach. This secretagogue effect together with the improvement of a number of ulcer patients induced the present study of mucilaginous substances. Hog's mucin, powdered okra, agar and olive oil were used inasmuch as they have a number of physical properties in common.

Tests were carried out on six normal young women, who had no gastro-intestinal complaints except possibly subject No. 4 who had a symptomless gastroptosis, on six patients affected with duodenal ulcer and on one dog with duodenal and

*From the Gastro-Intestinal Laboratory, Department of Physiology, the Department of Roentgenology and the Stomach Study Group, Michael Reese Hospital.
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harboring gastric cannulas. The emptying time of the stomach was determined fluoroscopically; intra-gastric digestion was followed by the Kestner method (3). The dog (female, 60 lbs.) had been operated upon one year ago and was in perfect health. She was kept on a constant diet during the tests.

METHODS

(1) *Fluoroscopy.* The normal subjects and the patients (14 hours without food) were given a barium-milk meal and for each individual the normal emptying time of the stomach was determined. Two days later, the same kind of meal with the addition of olive oil, agar, hog's mucin and okra, respectively, was given (4 c.c. or grams of the test substances, respectively). At the end of this series another control test with barium-milk alone was made. The observations made always agreed with these of the first control. At the beginning of each test, the entire bowel was examined with the fluoroscope in order to detect any possible constipation resulting from the barium of the previous test. In all cases scarcely any barium was detectable on the third day after a test. In order to check the results, the sequence of administration of the substances added to the barium meal was reversed with every other patient; in one patient the whole series was done twice, the second time with the sequence reversed. There was no difference in results irrespective of the sequence.

From the results of the above tests it was found necessary to compare the influence on emptying time of hog's mucin and okra, respectively, and therefore, on each of the six patients, one test with the okra-barium meal and another with the hog's mucin-barium meal was done.

(2) *Experiments on the Dog.* Food was withheld for 18 or 24 hours. Before each test the gastric and the duodenal cannulas were opened and allowed to drain for five minutes. If any food was found in the stomach, no test was done on that day. The duodenal cannula was then closed and 5 grams or 5 c.c. of the substance to be tested were placed into the stomach through the gastric cannula, which was then closed. Immediately afterwards, the dog was fed 250 grams of raw, fresh hamburger steak and 100 and 250 c.c. of water, respectively. The gastric cannula was opened one and a half and two hours, respectively, afterwards, and the stomach contents allowed to drain out. The solid and the liquid portions were measured separately in a graduated cylinder. Controls were carried out with a meat meal without test substance.

In the second type of digestion-motility test, the feeding and introduction of the test substances was done in the same way as in the first type. Then the duodenal cannula was opened and a thin rubber tube, 40 cm. long, was introduced into the distal jejunum through the duodenal cannula. The dog was in a Pawlow dog-stand and the rubber tube with a funnel at the end of it was held by a clamp on the upper part of the stand. After the meal, fluid and meat were discharged from the stomach in spurts and collected from the duodenal cannula under which a funnel and cylinder were placed. The number of spurts per 10 minutes was counted in order to give information concerning the opening of the pyloric sphincter as well as on the peristalsis of the stomach. The amounts of solid and liquid portions at the end of each ten-minute period were measured. The liquid fraction was passed through a fine wire mesh and then returned into the dog's jejunum through the rubber tube. This served to supply information respecting the amount of digestion in the stomach as well as the volume of secretion of gastric and duodenal juices. The liquid part was returned directly into the dog in order to interfere as little as possible with the digestive processes and reflexes.

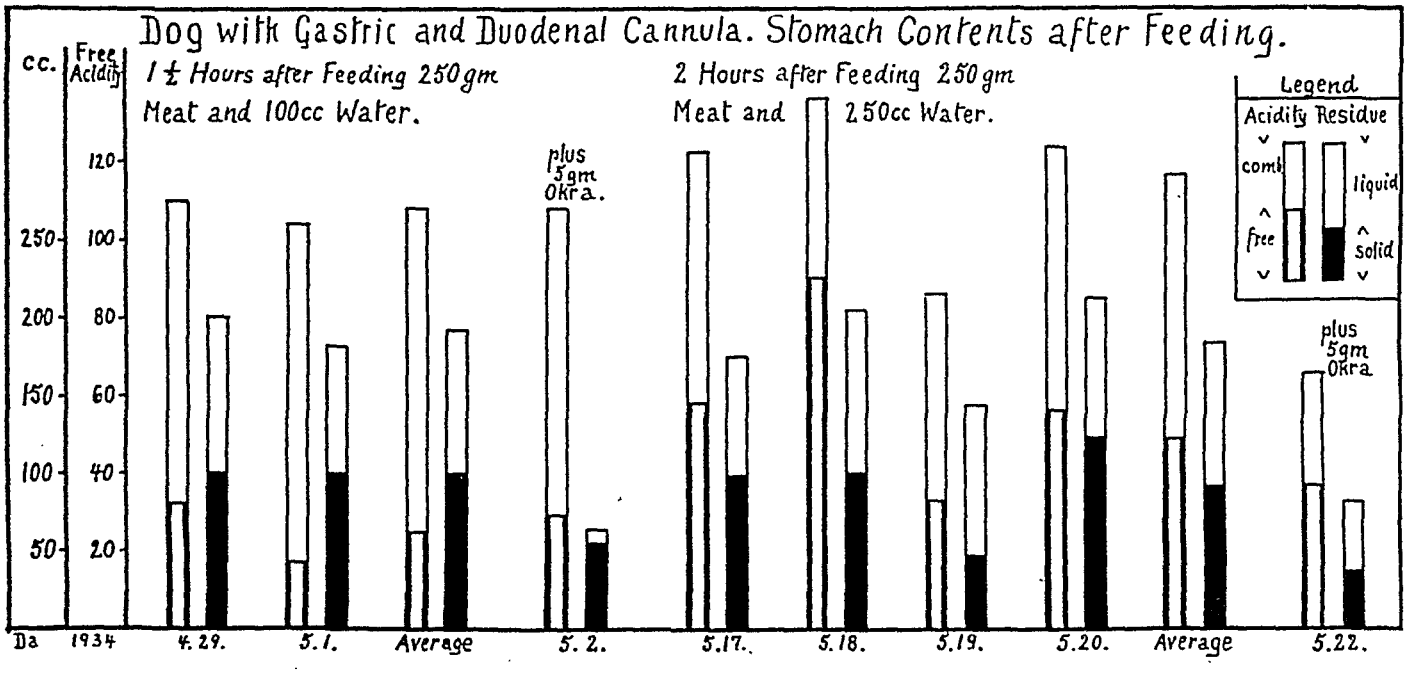
RESULTS

(1) *Fluoroscopy on Human Subjects:*

(a) The results in all six subjects were consistent (Table 1). Every tested substance decreases the emptying time of the stomach. Olive oil and agar produce a slight change; hog's mucin, a somewhat greater and okra a still greater. It is felt that only with this last substance is the decrease in emptying time sufficient to produce physiologic effects (22-48 per cent). It is noteworthy that during the first hour there was an actual delay in the emptying of the stomach but that, at the end of the second hour, a more rapid rate of emptying was noticed than that in the controls. This is substantiated by the results given in Table 2.

(b) At the end of the first hour after the test meal the hog's mucin-barium mixture left the

CHART I



stomach more quickly than did the okra-barium mixture (Table 2). At the end of the second hour the emptying rates were nearly equal; at the end of three hours the okra mixture decidedly was emptying faster; 96 per cent of the okra and 83 per cent of the hog's mucin mixture had left the stomach at that time. In three patients with the okra mixture the stomach was completely empty after 180 minutes; in one after 195 minutes, and in two after 200 minutes. The rate for hog's mucin in three patients, was 200 minutes each and in three others, 215 minutes. The averages are 189.2 minutes for the okra meal and 207.5 minutes for hog's mucin meal.

TABLE I

Emptying Time of Stomach in Minutes in Six Normal Female Subjects.

No. of Subject	Dates of Tests (1931)	Barium Control	Barium+ Olive Oil	Barium+ Agar	Barium+ Hog's Mucin	Barium+ Okra	Remarks
1	12-16 to 12-28	240	215	225	205	180	Okra emptied very slowly in 1st hour but rapid emptying at end of 2nd hour
2	12-16 to 12-28	250	225	230	205	195	Same
3	12-16 to 12-24	260	220	240	215	200	Same
4	12-16 to 12-21	310*	230	245	235	210	Same. *Not taken into average
5	12-16 to 12-21	240	210	215	205	185	Same
6	12-16 to 12-24	255	220	230	215	200	Same
Average		249	220	231	213	195	

Experiments on the Dog:

These tests were performed in order to check the results obtained on human subjects (Chart 1).

An ordinary meal was given; thus the use of barium was avoided and at the same time the process of digestion of food with and without okra could be followed. The first part of Chart 1 shows results obtained with one and one-half hours' digestion time. There was an average of 191 c.c. of the meal emptied, 100 gm. of which were solid meat and 91 c.c. were liquid. After the addition of 5 gm. of okra to the meal, a total of 63 c.c. was emptied, 55 gm. of which were solid and only 8 c.c. liquid. After two hours' digestion, the average of four control experiments was 185 c.c. total, of which 93 gm. were solid and 92 c.c. liquid. After okra the values were 82 c.c. total, 37 gm. solid and 45 c.c. liquid.

Chart 2. The vertical columns indicate the total volume emptied through the duodenal cannula in each 10-minute period. The white represents the volume of fluid, the black part the volume of solid. The interrupted line indicates the number of spurts in each 10-minute period.

TABLE II

Emptying Time of the Stomach in Six Male Patients with Duodenal Ulcers.

Patient No.	Barium Meal Plus	Time after Barium-Okra or Barium Mucin Meal in Minutes					
		60	120	150	180	200	215
		Per Cent Emptying of the Stomach					
7	Okra	10	50	80	100		
	Hog's Mucin	30	60	70	80	100	
8	Okra	15	60	80		100*	
	Hog's Mucin	35	60	80	90		100
9	Okra	10	50	70	100		
	Hog's Mucin	30	60		85	100	
10	Okra	10	50	80		100	
	Hog's Mucin	30	60	80			100
11	Okra	20	60		85	100	
	Hog's Mucin	35	60		80		100
12	Okra	15	50	85	100		
	Hog's Mucin	35	60		80	100	
Average	Okra	13.3	53.3	79	96.3		
	Hog's Mucin	32.5	60	76.7	83		

*Empty at 195 minutes.

The data on Chart 2 confirm the results obtained in man relative to the delay of the emptying of an okra-barium meal during the first hour after ingestion. There are no spurts for 10 minutes, then spurts for 20, and no spurts for another 30 minutes. The columns show the initial delay in emptying during the first hour and the rapid expulsion of food afterwards. The volumes are compared in Table 3.

TABLE III

Hour After Meal	SOLID				LIQUID				TOTAL			
	Controls			Okra	Controls			Okra	Controls			Okra
	1	2	Aver.		1	2	Aver.		1	2	Aver.	
1	86	39	63	8	278	266	272	71	364	305	335	79
2	120	55	88	89	276	373	325	206	396	428	412	293
3	30	56	43	140	164	248	206	153	194	304	249	293
Total of 3 hours	236	150	194	237	718	887	803	430	954	1037	996	665

Table 3. There is a distinctly less quantitative evacuation of solid stomach contents in the okra experiments during the first hour than occurred in the controls (8 and 63 gm., respectively). During the second and third hours, however, so much solid is emptied, that the total is nearly equal to that of the control (237 gm. versus 194 gm.). In no case, however, is the liquid in the okra test so great in volume as it is in the controls; only once (three hours) does the greater amount of solid account for it. The total liquid for the three-hour period of the experiment (consisting of digested and liquefied meat and digestive juices from the stomach and duodenum) is much smaller, nearly half, in the okra experiment than that in the controls (430 c.c. versus 803 c.c.).

DISCUSSION AND CONCLUSIONS

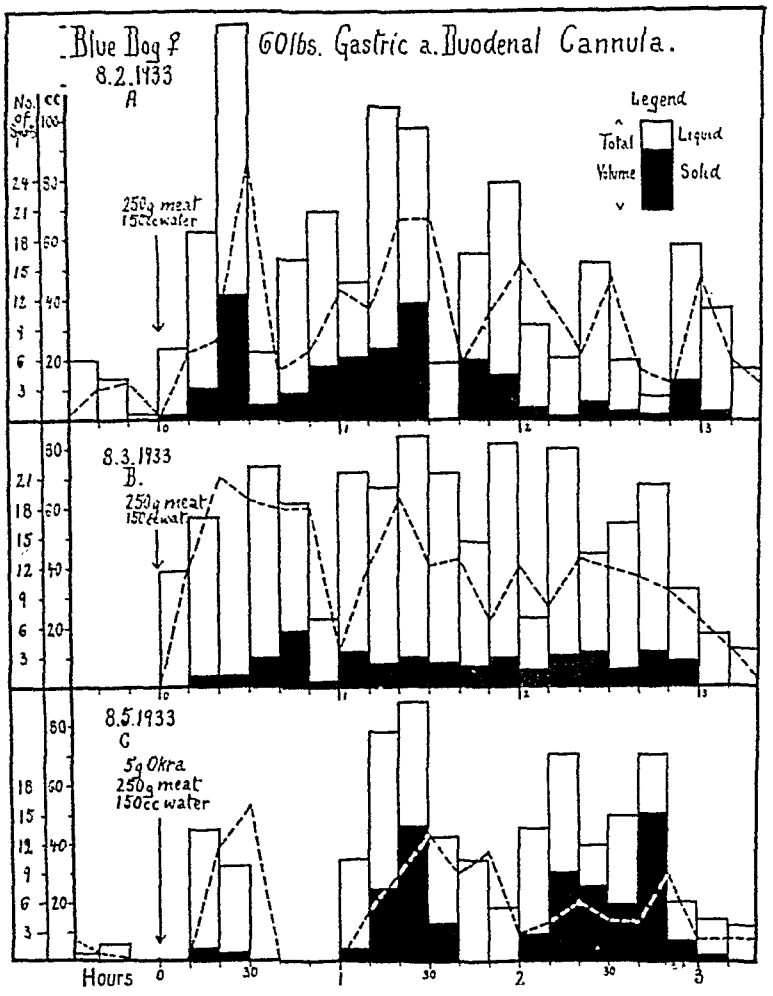
Small amounts of oily and mucilaginous substances decrease the emptying time of the stomach in varying degrees, but okra lessens it most definitely. The experiments, both on man and dog, clearly demonstrate this observation. In man the diminution is from 22 to 48 per cent, with an average of 26 per cent. The subject in which the decrease was 48 per cent exhibited a gastroptosis (without symptoms) and had an emptying time with the barium meal alone (control) of 310 minutes, as compared with 240-260 minutes in the five other subjects. Yet all tested substances reduced the emptying time of this stomach to the average of the emptying times of the other persons of this group.

From the group of normal persons and the group of patients affected with peptic ulcer, it is seen that there is a delay of emptying during the first hour after an okra-barium meal, and afterwards a speeding up which not only compensates for the loss but shortens the emptying period of the stomach as compared with the controls. After hog's mucin there is relatively rapid emptying during the first hour and then a slower rate during the third hour.

In the dog, there is a 50 per cent greater degree of digestion of a meat meal with okra than the same meal without okra; one and a half and two hours, respectively, after feeding. The diminution in the volume of fluid is still greater and amounts to 8 c.c. versus 37 c.c. and 45 c.c. versus 92 c.c. in the controls (Chart 1). From Chart 2 and Table 3 the same can be concluded. The three-hour volume of solid is 194 gm. (average of two experiments) for the controls and 237 gm. for the okra meal. The values for liquid are 803 and 430 c.c., respectively. The tests represented in Chart 1 seem to follow more closely normal physiological conditions and, therefore, are more informative. The initial delay in the emptying of solids after okra may explain the greater degree of digestion noted in the experiments detailed in Chart 1. The diminution in the amount of fluid after okra can be explained only by decrease of gastric secretion, because there is observable no impairment of liquefaction and digestion of meat.

In Chart 1 the free and combined acidities are within the limits of the controls; the combined acid practically is the same as in the controls in the one and one-half hour okra test and less than in the controls in the two-hour test. Although in previous studies (2) an increase of gastric acidity was found after okra only, apparently this cannot be expected after a meat-okra meal.

CHART II



At present it is not possible to explain the mechanism responsible for these findings. It is conceivable, from analogous experiments, that okra contains a substance which is activated during digestion and then slowly increases the peristalsis of the stomach. An extract of okra with saline or alcohol, when injected intravenously in a dog under ether, lowers the blood pressure in a histamine-like manner. It is not possible either to explain why dog's mucin at first speeds up gastric emptying time and then slows it. In conformity with the above assumption with respect to okra, it is possible that peristalsis-stimulating substances are available in hog's mucin and are absorbed immediately after ingestion.

This work was undertaken in order to explain the reason for certain beneficial effects of mucilaginous substances upon peptic ulcer. Because okra had the most decided effects its study was entered into in more detail. It is difficult to say how a delay in emptying time benefits an ulcer patient. Perhaps in such circumstances the food proteins can bind more of the secreted acid and soft food may protect the mucosa during the mixing process. The shortened emptying time (Ta-

bles 1 and 2) in the third hour and the decrease in the total amount of secretion as well as the complete digestion of meat, may explain the favorable effect of okra in some cases of peptic ulcer. Although okra increases the acidity of the stomach contents (2), nevertheless, in view of the decreased volume of total secretion, the acid may be neutralized more easily by mucus, regurgitation from the duodenum and food in the stomach; thus it is quite possible that one effect neutralizes or even overneutralizes the other. The initial delay of emptying time after okra may be beneficial also by allowing the stomach to remain filled while the intestinal phase of gastric secretion is beginning, so that the acid secreted then can be bound by the buffers in the food. It would seem logical to assume that okra would have its optimum effect when it is given simultaneously with the meals of a proper diet.

SUMMARY

The effect of hog's mucin, okra, olive oil and agar were tested on the motility of and the digestion in the stomach. Tests were performed on six normal subjects, on six patients affected with peptic ulcer and on a dog carrying both gastric and duodenal cannulas. While all of the test substances decreased the emptying time of the stomach, okra had the greatest effect. At the beginning of digestion, hog's mucin increases and okra decreases gastric motility. After three hours, this is reversed, and okra diminishes the emptying time by 26 per cent. In the stomach okra does not impair the digestion of meat; it considerably decreases the amount of gastric secretion. The therapeutic significance of these results is discussed.

ACKNOWLEDGMENT

We wish to thank Mr. A. Pilon for his valuable technical assistance.

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Studies on the Gastric Hunger Mechanism*

By

IRA A. MANVILLE, M.D.

and

ELDON G. CHUINARD, Ph.D.

PORTLAND, OREGON

IT IS well known that hunger in the normal individual is associated with strong contractions on the part of the stomach. Coincident blood sugar determinations show that this substance is present in the blood in amounts within the lower limits of normality. On the contrary, the hunger manifested by individuals suffering from diabetes mellitus is associated with high blood sugar levels. Furthermore, the motility of the stomach during gastric digestion seems to be uninfluenced by the steady rise in blood sugar occurring as a result of the absorption of glucose from the intestine. The dietetic procedure of administering a small amount of sweet food a half hour before mealtime in order to reduce the pangs of hunger seems to indicate that sugar in the stomach or in the small intestine has an influence on the hunger and appetite mechanism.

Psychic control of gastric secretion *via* the vagi appears to be well established. Excitation of these nerves also causes increased motility of the stomach. The vagi appear, therefore, to contain at least two sets of fibers: one responsible for the activation of the secretory elements and the other for the initiation of motor activity. Whether or not these two activities can be dissociated is not clear. Is the production of appetite juice invariably associated with increased motor activity? Are hunger contractions always accompanied by a copious production of gastric juice?

Although much experimental work has been done toward unraveling the tangle which exists in regard to gastric activity, there still remains much to be known before a complete understanding of this mechanism can be had. Bulatao and Carlson (1) stated that the intravenous administration of glucose to dogs stopped hunger contractions resulting from food restrictions. Templeton and Quigley (2) claimed that "intravenous injections of dextrose not preceded by insulin, in amounts as great as 50 grams, usually produced in fasting animals no detectable modification in the motility of the Heidenhain pouch, although a simultaneous record showed that the motility of the main stomach was inhibited in the characteristic manner". Later these same authors (3) wrote, "In normal animals intravenous injections of dextrose produce only a transient gastric inhibition, and activity returns while the blood sugar and especially the glycogen reserve is well above normal". This statement was further revised

*From the Department of Physiology, University of Oregon Medical School, Portland Oregon.
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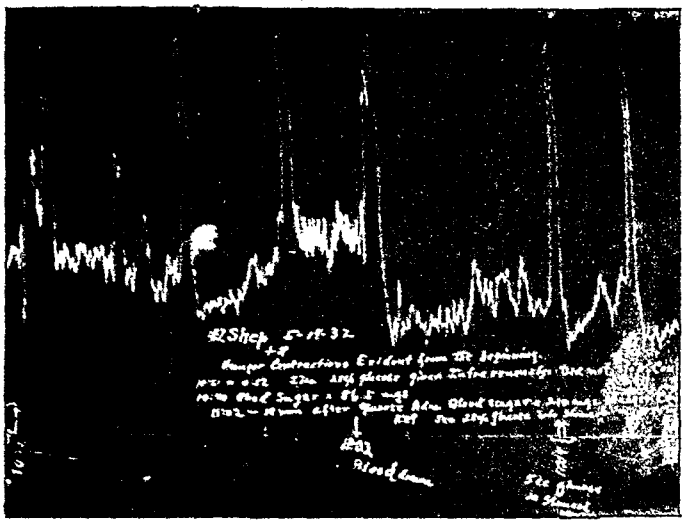


Fig. 1. Gastric motor record of "Shep" after 24 hours' starvation. Powerful contractions were evident from the outset. At 10:40 the blood sugar was 86.5 mgs. At 10:51, 27 c.c. of 25 per cent dextrose were injected intravenously. No effect noted. At 11:02 blood sugar was 210 mgs.

when Quigley and Hallaran (4) stated that, "In normal animals the effect on gastric motility of intravenous injections of glucose in quantities ranging from 1 to 25 grams was without immediate effect on spontaneous gastric motility. Occasionally a transient gastric inhibition was obtained just before, during, or after the injection. Such inhibition appears to be entirely incidental". Mulinos (5) claimed that the intravenous administration of glucose solution was without effect on the "hunger curves" and the "after feeding curves". In view of these considerations it seemed worth while to add our experimental data with the hope that additional evidence would help to clarify the situation.

AUTHORS' STUDIES

Methods—An ileo-gastrostomy was produced in three dogs.* They were fed the Cowgill vitamin B deficient diet (6). Yeast was added to this diet when it was not desired to study the effects of vitamin B deprivation. Before each experimental period food was withheld for 24 hours. The dogs were trained so that they would lie quietly on a table for as long as five hours. Through the fistula was placed a rubber tube on the inner end of which was a balloon. The outer end was attached to a chloroform manometer whose float was arranged to record pressure variations on a revolving smoked drum. A catheter with the closed end perforated with many medium-sized openings was also inserted into the stomach through the fistula. The outer end of the catheter was kept closed between operations by a spring clamp. At five-minute intervals the clamp was removed, the gastric contents aspirated and 50 c.c. of warm tap water introduced. The pH of the material removed from the stomach was determined colorimetrically. Ten c.c. quantities of the same material were titrated against N/40 NaOH to determine the free and total acid. At strategic intervals, samples of blood were withdrawn and sugar determinations performed, using the Schaeffer-Hartmann method and, later, the Somogyi modification of this. The amount of gastric contents aspirated was recorded. Variations in this gave some information concerning gastric tonus and motility as will be seen in Chart I.

*Animals prepared in this manner remain normal in all respects. We have maintained such animals for over three years.

For the sake of brevity, only *typical experiments* will be cited.

I—The determination of the effect of intravenous and of intra-gastric injections of glucose on the motility arising in the stomach as the result of food restriction.

"Shep" exhibited strong hunger contractions as soon as the apparatus was set up at 10:00 A. M. Powerful contractions occurred about every two minutes. These contractions were superimposed upon an elevated tonus rhythm. At 10:40 A. M. the blood sugar was 86.5 mgs. Eleven minutes later 27 c.c. of 25 per cent dextrose solution were given intravenously. No effect on hunger contractions was noted in the following 20 minutes of observation. At 11:02, or 11 minutes after the administration of the sugar, the blood sugar was 210 mgs. and the hunger contractions were unimpaired. It will be noted from Fig. 1 that the pain or discomfort usually associated with intravenous manipulations was not severe enough to cause a reflex stimulation of the adrenals with a resultant inhibition of gastric activity. Another figure will show that the hunger contractions induced by subcutaneous injections of insulin are stopped within a few minutes by the intravenous injection of sugar.

Twenty minutes after the intravenous administration of dextrose, there being no reduction in gastric motility, 5 c.c. of 25 per cent dextrose solution were placed in the stomach. In five minutes this was followed by 10 c.c. and after another interval of six minutes by 13 c.c. more. Altogether 28 c.c. of sugar solution were placed in the stomach over a period of 11 minutes. Within two minutes of the last injection and 13 minutes of the first, the hunger contractions were entirely stopped and gastric tonus considerably reduced. The stomach remained in a quiescent condition during the remaining 23 minutes of observation. Sixteen minutes after the last injection of sugar, the blood sugar was 175.5 mgs. (Fig. 2).

Comment: From this demonstration it may be seen that hunger contractions may occur spontaneously with a blood sugar at 86.5 mgs.; that they persist with a blood sugar at 210 mgs, and that they can be made to stop by introducing a small amount of sugar into the stomach, although the blood sugar still remains high—175.5 mgs.

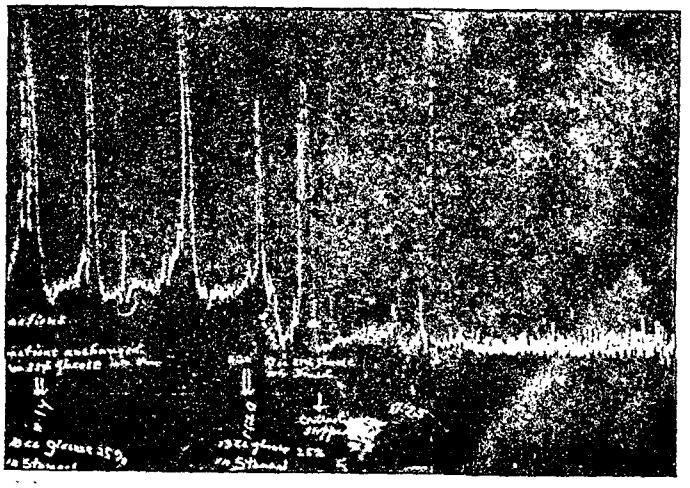


Fig. 2. Cessation of motility and drop in tonus resulting from placing 25 per cent dextrose solution into stomach. Blood sugar during early part of quiescent stage, 175.5 mgs.

Fig. 4. At 2:05 P. M. tonus markedly increased and motility at maximum 67 minutes after the intravenous injection of 27 units of insulin. At 2:10, 10 c.c. of 20 per cent glucose was placed in the stomach. Motility and tonus dropped immediately and within five minutes was negligible.

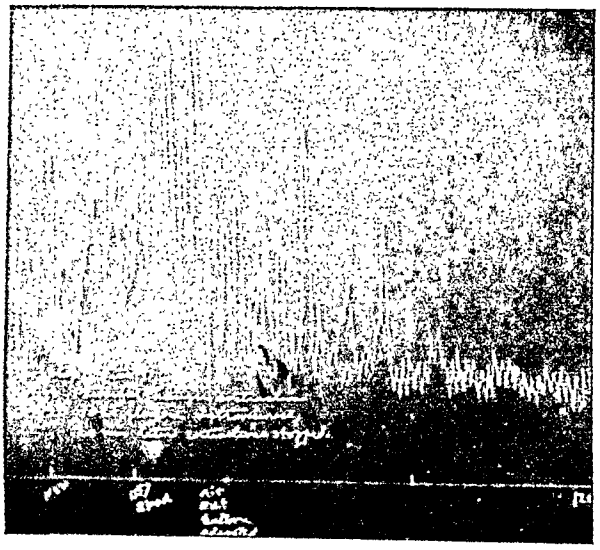
This latter inhibition is preceded by a latent period the full significance of which is not known. It may be due to the time required by the sugar solution to reach the duodenum. The inhibition appears to be influenced by the quantity and the strength of the solution introduced into the stomach.

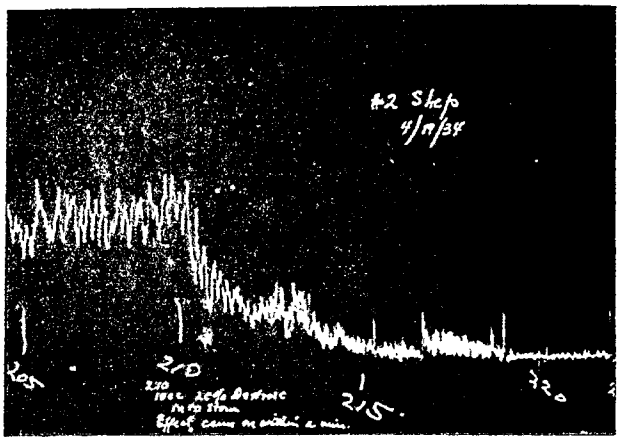
II—The determination of the effect of intravenous and of intragastric injections of dextrose on the motility arising in the stomach as a result of insulin injections.

"Shep" exhibited powerful hunger contractions 22 minutes after 22 units of insulin were given subcutaneously. At 11:42, in the midst of strong contractions, 10 c.c. of 25 per cent dextrose were given intravenously. Seven minutes later there was a marked drop in motor activity and within the next six minutes activity had almost completely stopped. This effect lasted a little over 15 minutes (Fig. 3).

At another time "Shep" received 27 units of insulin intravenously. Sixty-seven minutes later the blood sugar was down to 59 mgs. and the stomach was showing maximum activity. Twenty-two minutes later 10 c.c. of 20 per cent dextrose solution were placed in the stomach with an immediate drop in tonus and motility. At this time, with a quiescent stomach, the blood sugar was found to be 57 mgs.—only 2 mgs. different from the value found during maximum activity (Fig. 4). Twenty minutes later the tonus was going up.

Comment: In contrasting the results of this demonstration with those of the preceding one, attention must be drawn to the fact that in the hypermotility induced by insulin, inhibition is produced in 13 minutes by the intravenous injection of 10 c.c. of 25 per cent dextrose solution while in spontaneous hypermotility the intravenous injection of 27 c.c. of a similar solution was without effect. The difference in latent periods





following intragastric injections of sugar solutions can be ascribed to differences in initial tonus of the stomach and perhaps to differences in the quantity and concentration of the sugar solution. In keeping graphic records of the type pictured in Chart 1 it has been noted that when the tonus is extremely low in the stomach or when tonus and motility are high, fluids introduced into the stomach are quickly discharged into the intestine. Only when the tonus is moderate is there an appreciable delay. It appears from such records that for fluids to reach the intestine quite soon after their introduction into the stomach, gastric tonus and motility must either be great enough to overcome the tonus of the pylorus or the tonus of the stomach must be low enough to involve that of the pylorus also.

This experiment brings out the point that there is an essential difference in the hunger contractions produced by food restriction and those resulting from the administration of insulin in that the former are uninfluenced by the blood sugar level while the latter are. By varying conditions, hunger contractions can be produced at blood sugar levels of 59 mgs. or of 210 mgs. This seems to prove beyond doubt that hunger contractions are not directly related to the blood sugar level.

III—The determination of the effect of vitamin B deficiency on the motility of the stomach of normal and of insulinized dogs.

For some time a deficiency of vitamin B has been known to cause anorexia. The use of insulin in non-diabetic malnutrition made it seem advisable to determine the effect of this hormone on gastric motility when the experimental animal was exhibiting the anorexia of B-avitaminosis.

On January 7, 1932, "Shep" was placed on the Cowgill vitamin B deficient ration. Her initial weight was 32.5 pounds. Eighteen days later she stopped eating (loss of appetite) although gastric motility (hunger contractions?) could still be evoked with insulin. Fifty-two days

Fig. 3. Powerful hunger contractions were in evidence 22 minutes after the subcutaneous injection of 22 units of insulin. At 11:42 A. M., 10 c.c. of 25 per cent dextrose was injected intravenously. Motility and tonus both reduced within 13 minutes.

after the initiation of the diet no motility could be produced with insulin, although the blood sugar was reduced to 46 mgs. (Fig. 5). Two days after the failure to produce an increase in gastric motility with insulin injections, a glucose tolerance test was performed. Three days after this extreme prostration with mild convulsions and vomiting appeared so that it was considered advisable to administer small amounts of vitamin B over a period of three days. Up to this time "Shep" had lost seven pounds or 21.5 per cent of her original weight. Within three days of receiving the vitamin supplement her appetite was restored so that she ate all her food, although gastric motility resulting from injections of insulin was not fully re-established when a trial was made three weeks after the yeast addition was begun. Similar results were obtained with a second dog. Hunger contractions could not be elicited with insulin, although the blood sugar was reduced to 54 mgs.

Comment: It appears from these results that insulin is powerless to evoke hunger contractions in animals suffering from a deficiency of vitamin B, although the blood sugar is still capable of being lowered. Furthermore vitamin B seems to be able to restore appetite before it does that of gastric motility. It would not seem, therefore, that appetite is dependent upon gastric motility.

There seemed to be such a marked difference in the response to insulin of normal and of B-avitaminotic dogs that it seemed advisable to determine their glucose tolerance. "Shep" (B-avitaminotic) and "Curley" (normal) were each given intravenously 1.75 grams of dextrose per kilogram of body weight. Blood sugar determinations were made prior to the administration of sugar and at half-hour intervals thereafter until eight samples had been withdrawn. The blood sugar of the normal animal showed very little if any fluctuation—never exceeding the initial level. The blood sugar of the vitamin B deficient dog mounted to 205 mgs. at the end of the second hour and was still above the initial level at the end of four hours. In the former animal the urine remained negative for sugar while that of the latter animal became strongly positive. It seems, therefore, that a deficiency of vitamin B is capable of producing a glucose tolerance curve very similar to that existing in diabetes mellitus. We are inclined to feel, however, that this condition is not due so much to the deficiency of vitamin B directly as it is to the resulting loss in appetite and the consequent lack of glucose producing materials in the intestine (7, 8).

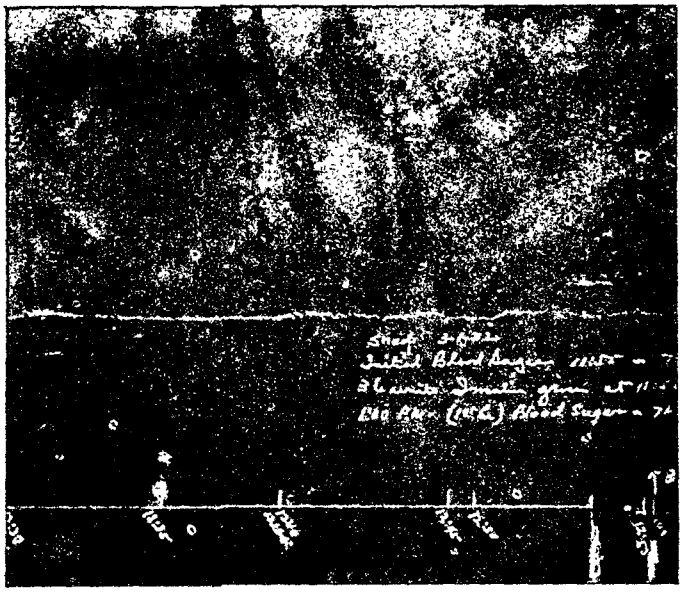


Fig. 5. Gastric motility and tonus in dog suffering from vitamin B deficiency. Although 36 units of insulin reduced the blood sugar to 46 mgs. no increase in tonus was noted and motility failed to develop.

IV—Is gastric motor activity invariably associated with secretory activity?

In earlier work there appeared indications that there existed a dissociation of the secretory and of the motor activities of the stomach. In order to determine this point more carefully a series of experiments was performed in which this point became the definite objective.

"Shep" with an initial blood sugar at 1:20 P. M. of 86 mgs. was given 27 units of insulin subcutaneously. One-half hour later there occurred a marked increase in acid production without any change in muscular activity. One hour later there occurred a definite increase in tonus and motility. At the height of gastric secretory and motor activity, 10 c.c. of 25 per cent dextrose solution were placed in the stomach with the result that the acid production showed an immediate reduction. There was a latent period of four minutes before tonus and motility declined. The production of acid continued to decline for the remaining 14 minutes of observation while tone and motility began improving after five minutes of quiet and were fully restored in seven minutes (Chart I).

Comment: The influences controlling the production of acid seem much more sensitive to experimental conditions than those regulating motor activity. Increases in acid occur before those of muscular activity; they are inhibited earlier and for a longer time than motility. It would seem, therefore, that they are not inseparable.

CONCLUSIONS

1. Hunger contractions are not directly related to the blood sugar level.

2. Gastric motility resulting from food deprivation or from insulin administration can be stopped by placing a dextrose solution in the stomach. Only the activity induced by insulin can be stopped by dextrose intravenously.

3. Insulin is not capable of producing hunger contractions in animals suffering a deficiency of vitamin B.

4. Either a deficiency of vitamin B or the resulting lack of food materials in the digestive tract causes a decreased tolerance for dextrose.

5. There is a dissociation in gastric activity between secretion and motility. Secretion has been observed to decline while motility was increasing.

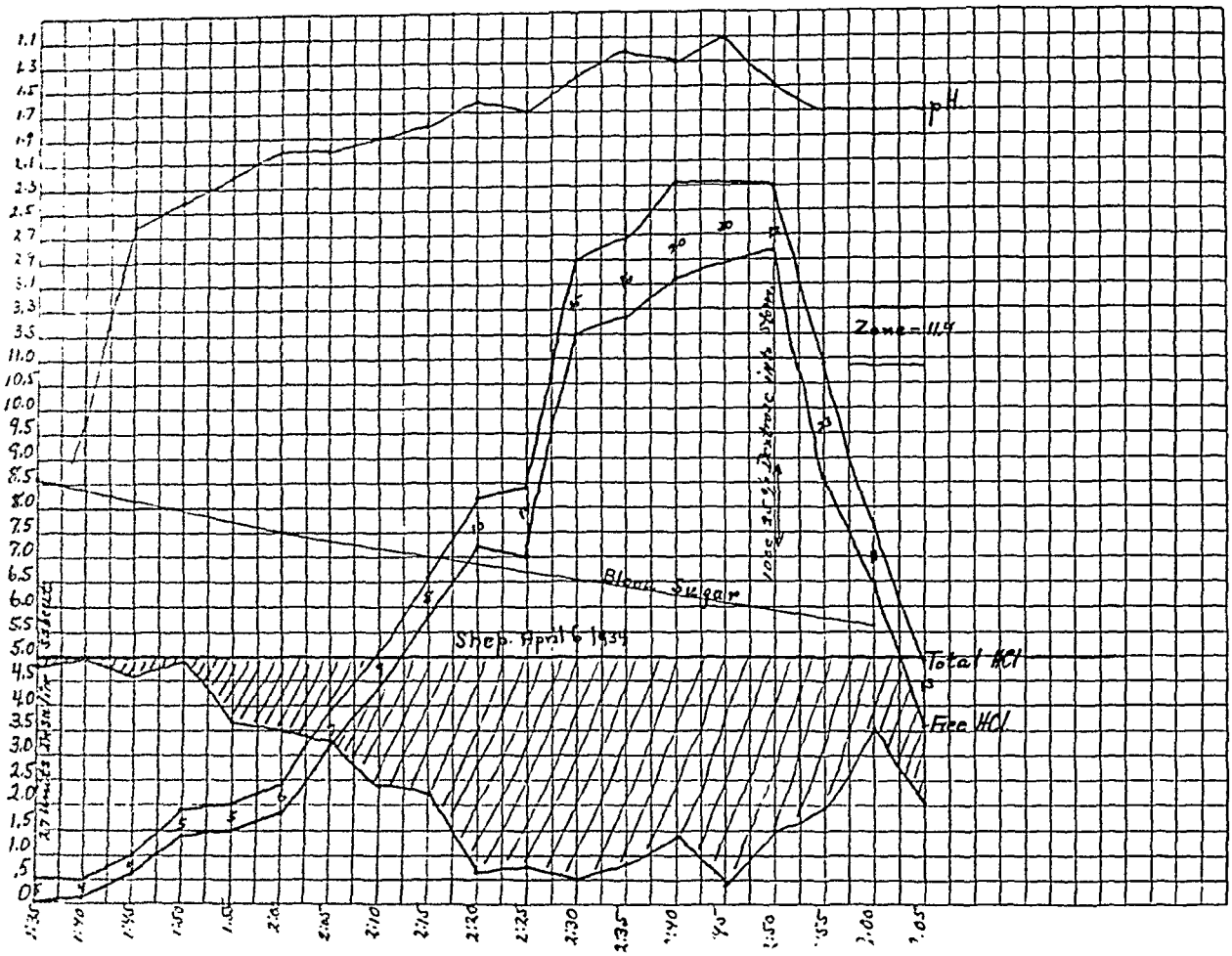


Chart 1. The upper line represents the pH of the gastric samples removed every five minutes. The highest acidity was reached 70 minutes after the injection of the insulin. The sharp drop in acidity at 2:50 and 2:55 illustrates the marked inhibitory effect of the intragastric injection of dextrose solution. The blood sugar curve shows an initial blood sugar of 86 mgs. with a terminal blood sugar of 56 mgs. The free and total acid curves show a rapid ascent during the half hour between 2:00 and 2:30. The next 20 minutes represents a moderate increase in production. The introduction of sugar into the stomach caused a very rapid decrease. The production of acid increased in the face of a falling blood sugar. The figures lying between the free and total acid curves represent the differences, that is the number of c.c. N/40 NaOH taken up by the buffering substances in the gastric juice. The average buffering value was 11.4. Values below .05 are not significant since they can be accounted for on the basis of color change in the two different indicators. There is enough buffering material in 10 c.c. of the aspirated gastric contents, therefore, to combine with 11.35 c.c. N/40 alkali. HCl was produced earlier than appreciable amounts of buffer substance. The heavy line drawn at level 5.0 (50) represents the 50 c.c. portions of water placed in the stomach at five-minute intervals. The cross-hatched area represents the amount of material removed from the stomach during the same intervals. As tonus and motility increased less material was aspirated because of its escape during the interims into the duodenum. At 2:50 when the sugar solution was placed in the stomach it will be noted that motility and tonus decreased as well as acid production. At 3:00, however, motility was increasing while acid production still continued downward. The graphic motor record of the stomach shows this still better.

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Carcinoma of the Colon*

By

CHARLES W. HEALD, M.D.
BATTLE CREEK, MICHIGAN

A REVIEW of an ever increasing literature on cancer of the colon impresses one that no phase of this subject has been neglected. Experience in gastro-intestinal work also leads one to conclude that malignancy of the colon develops very insidiously so that at the time of discovery it is often too late to accomplish much in the way of treatment. For this reason we must keep definitely in mind that cancer is on the increase and statistics tells us that one out of every seven people will die of cancer located somewhere in the body.[1] It therefore is most important that the general practitioner or specialist whom the patient consults be ever watchful for any unusual gastro-intestinal symptoms and not be satisfied until a correct analysis has been made, especially if the symptoms are not relieved promptly by proper therapeutic effort.

Cancer of the colon is like cancer in any other part of the body. It is a local disease at first and usually does not produce early symptoms that are pathognomonic or develop physical signs that would lead to an early diagnosis. So, often patients are not incapacitated for work when their attention is attracted by the development of symptoms that are more or less alarming and that finally send them to a physician for consultation. Failure by regular therapeutic efforts to relieve symptoms such as gas, constipation, indigestion, loss of weight, occasional attacks of diarrhea, should call for thorough investigation of the case by proctoscopic examination, x-ray and stool analysis.

A review of one hundred cases reveals the fact that the average age is fifty-eight years; sixty-five were males and thirty-five females. Twenty-five per cent had a definite diarrhea, passing from five to eight stools per day, usually containing blood and mucus. Thirty-eight per cent had constipation sometime during the course of the disease, generally in the early stage, frequently alternating with diarrhea. Forty-nine per cent had blood in the stool. Gas was prominent in thirty-nine per cent; abdominal pain in forty-five per cent. The average loss of weight was thirty pounds and the duration of the symptoms was nine months.

SYMPTOMS

The symptoms might well be divided into two groups, *early* and *late*. It is the concensus of opinion that lesions of the cecum and ascending colon produce the fewest symptoms, while in the descending colon and sigmoid the symptoms are more prominent. The early symptoms common to all parts of the bowel are: vague indigestion, anorexia, gas in stomach and bowels, weakness, tired feeling, constipation and loss of weight. Late symptoms are: obstruction, partial or complete, palpable mass, pain, vomiting and bloating, constipation alternating with diarrhea, with blood and mucus in the stool.

*Department Internal Medicine, Battle Creek Sanitarium.
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Rayford states that the average *duration of symptoms* is about fourteen months, Hurst nine and one-half months. As mentioned previously in this paper, the average in the one hundred cases reviewed was nine months.[2]

Physicial signs are negative in the early stage of the disease, usually only a moderate distension may be observed. However after the lesion has developed to the degree of producing definite symptoms, one may be able to palpate a *tumor* in a small percentage of cases. In the one hundred cases reviewed, physical examination was positive in thirty-two cases.[2] The patient is generally pale and has a moderate secondary *anemia.* The blood picture differs with the location of the lesion. It is a well established fact that secondary anemia is more marked with right side tumors than with left. The tumors of the cecum in this series showed a red cell count of 3,450,000; ascending colon 3,386,000; transverse colon 4,023,000; descending colon, sigmoid and pelvic loop 4,219,000 per cubic millimeter. The average for the cecum, ascending and transverse colons was 3,619,000 per cubic millimeter, which is in harmony with practically all statements in the literature that the secondary anemia is more marked in right side tumors.

A reason suggested for the secondary anemia is that the cancers of the right colon are usually larger, offer a larger ulcerated surface, making it possible for more hemorrhage to occur. The anemia is not due to any intrinsic property of the growth itself, but to the fact that absorption of fluids in the right colon is much more common than in the left colon and consequently the effect of the greater absorption of hemolytic toxic products from the necrotic cancer of the right colon is more marked.[4]

W. J. Mayo[5] stated that the purpose of the proximal colon is to remove nutritive material from protein, fats and carbohydrates. The unabsorbed end-products which undergo putrefaction and fermentation make it possible for the toxic products to develop—the influence of which may result in a very definite secondary anemia.

The only hope of reducing the mortality resulting from cancer of the colon is a careful analysis of early symptoms. This, of course, will depend upon the ability of the practitioner to evaluate extremely vague symptoms and insist upon a careful and extensive study of the case and continuous observation of the same. According to Hurst:[6] "The two earliest symptoms are abdominal pain or discomfort and change in habitual action of the bowels. This discomfort will always be present in the segment of the bowl proximal to the developing obstruction. It will be a small insignificant pain located, for cancer of the cecum, in the region of the umbilicus; in ascending colon and hepatic flexure, on the right side of the abdomen; for splenic flexure, descending colon and sigmoid, on the left side of the abdomen. Pain produced by a lesion of the transverse colon will be felt below the umbilicus and pain resulting from cancer in the pelvo-rectal region will be located between the umbilicus and the pubes." The pain is frequently colicky, relieved by a passing gurgle, which often enables a patient to assist very greatly in locating the lesion.

Sooner or later the majority of the cancer cases will show some discrepancy in bowel action. For a time it may be either constipation, diarrhea or both. When a patient has such a history this is always significant, especially if blood or pus is present, and should be considered a potential case of cancer until proven otherwise. Mucus with a solid stool is insignificant but if associated with liquid or semi-solid stools, would suggest an ulcerative colitis. However if fragments of solid feces are present with the diarrhea, this would suggest a lesion of the lower colon. Visible blood and pus are seldom present when proximal to the pelvic colon. For lesions higher up one must always rely upon rather delicate blood tests as the guaiac reaction and spectroscopic test.

Three groups of symptoms characterize carcinoma of the *right half of the colon:*

Symptoms of indigestion extending over a long period. Symptoms of irritability that are preferable to the right ileac fossae and gall bladder. Slight tenderness may be present.

Slow progressive secondary anemia without visible loss of blood.

Discovery of a tumor, on the right side of the colon, by the patient himself or in regular routine examination. This comprises about ten per cent.

The *left side* presents a group of symptoms largely due to obstruction resulting from stenosis of the lumen.[7]

LOCATION

These hundred cases which I carefully reviewed were all diagnosed in the usual way by taking careful case history, physical and proctoscopic examination and by the use of the Roentgen ray. Many were confirmed by surgical operation.

The stomach is often considered the most frequent site of carcinoma, but the large intestine, including the rectum, taken as a system, produces more cancers than does the stomach itself, but the number of lesions as to location in the different parts of the gut will differ somewhat with each observer.

Embryologically, the colon has its origin in the left side of the body and the small intestine in six primary convolutions on the right side. At about the eleventh week the embryonic colon begins to move to the right and continues to move until the head of the colon reaches its normal situation soon after birth. The right half of the colon originates with the small intestine from the mid gut, having in the embryo the same villi and it retains the same blood supply from the supermesenteric vessels as the small intestine.

Inasmuch as the clinical picture is somewhat

different resulting from lesions from cecum to splenic flexure, commonly designated as the right colon, and lesions occurring in the descending colon and sigmoid, for convenience sake we will speak of them as right and left colon. As stated above, forty-one per cent of the neoplasms occurred from cecum to splenic flexure, the majority occurring in the cecum, ascending and transverse colons. The colon possesses the flexity and has some of the absorbtive properties of the small intestine. Therefore large growths can exist in the right half of the colon without resulting in at least early obstruction.[8]

Adenocarcinoma is the type of growth that is most commonly found in the right colon, practically to and including the hepatic flexture, while in the transverse colon the tumors assume the anular constricting form sometimes designated as the "napkin-ring" carcinoma.[9]

The growth begins as a small ulcer on the mucosa of the gut wall. The edges are hard and elevated, leaving a crater-like erosion in the center. The wall becomes thickened and indurated as the growth develops around the wall as well as longitudinally. It eventually produces an anular growth which always has a marked tendency to produce a high grade of obstruction.

Metastases from this lesion may involve mesentery glands, liver, stomach and other adjacent organs. It has been observed that tumors in the cecum and ascending colon do not metastasize so readily. The descending colon or left colon has primarily a storage function. Here absorption is nearly complete. Excreta is dehydrated and more solid. The function therefore is practically storage.

In a paragraph above it will be noted that the greatest number of neoplasms occur in the large intestine, including the rectum as a system. The type of tumor found in this area is the hard or scirrhous, rather than the soft tumor, finally resulting in a high grade of obstruction.[10]

THE ROLE OF POLYPOSIS

The term polypus is an anatomic or morphologic term applied to a form of growth arising from any of the tissues constituting walls of the stomach or intestine. The frequency of occurrence of simple or multiple polyps of the large intestine or rectum will always be in proportion to the care and application one seeks for them. They are most always present in specimens removed surgically, often found at the mortuary table and often seen at proctoscopic examinations. Their size and number are variable but one can usually demonstrate small protuberances from mucous membrane, which histologically are true polyp formation, to the diffuse lesion commonly known as "polypoidosis" of Broder. These project from the mucous membrane of the organ and being constantly tugged upon by the bowel content, resulting from peristaltic movements, they frequently develop a pedicle from which the mass is suspended. These growths may vary in size from a small lentil to that sufficiently large to obstruct the bowel.

It is stated by observers that polypoid involvement may extend through the entire gastro-intestinal tract, from cardia to anus.[11] Anderson and Tavell state they are more commonly found in stomach and colon and may occur at all ages from childhood up, but more commonly from forty to fifty years of age. The tissue from which these masses have their origin will decide very largely the future influence they will have on the mechanism.

The polyadenomata constitute a definite group and they are of epithelial origin, arising from under the mucous membrane, being exposed to irritation and inflammatory reaction affecting the membrane, thus having a tendency to malignant changes.

Polypoidosis of the colon has been known since Virchow's time, he making the discovery and recording it in 1863, as colitis polyposa. This was elaborated upon by Cripps in 1882. In reviewing three cases he described accurately the condition now known as polypoidosis. This term indicates that the entire lumen of the bowel from anus to cecum presents a roughened elevated site interspersed with small normal areas giving it the appearance of brain convolutions.

Another school of thought leans toward heredity and congenital tissue "rests," putting forth the argument that these characteristic growths develop in youth in which their years have never given ample time for irritation and no history of inflammatory reactions.

This is called the congenital type of polypoidosis and is recognized as a precursor of malignant growth in a high percentage of cases. The congenital type manifests itself in young persons by profuse rectal hemorrhages and diarrhea, associated with anemia and occasionally acute intestinal obstruction.

Cripps' first patient was a male, age twenty years, with symptoms for ten years and polyps had been removed by way of the rectum with only temporary relief. This patient died suddenly and post-mortem examination showed that death had occurred because of diffuse pedunculated polyps.

Later he reported two other cases, brother and sister of the first patient, seventeen and sixteen years respectively.

Erdman reported two cases, one fourteen and one sixteen years of age.

Niemack reported the case of the youngest patient on record, a girl aged twelve years, who had been ill for three years. The diagnosis of congenital polypoidosis is usually made by digital or proctoscopic examination because the polyps involve the rectum as well as the entire colon.

Polyps of the large bowel according to Rankin[12] are described as pedunculated or sessile growths with an adenomatous base. Their presence in the colon and rectum are of more significance as regards the ultimate development of

cancer. They occur four times more often in the large bowel and rectum than any other part of the gastro-intestinal tract. Pathologically there are two general types of polyps in the colon, one a true neoplasm designated as polypoidosis congenital. It is believed that fifty per cent of these cases may become malignant. The acquired type is that which most often occurs in adult life that may be associated clinically or etiologically speaking with dysentery, ulcerative colitis, hyperplastic tuberculosis, or non-specific infections of the large bowel.

Chronic ulcerative colitis has been complicated by the formation of polyps finally resulting in malignancy. This is rare, but infrequently, to be sure, it does happen. The theory of irritation enters into this phenomena. If irritation in the viscus elsewhere in the body develops a fertile soil for malignancy, it would seem very reasonable to believe that a long-standing, recurring, progressive ulcerative colitis might be a factor in malignancy.

DIAGNOSIS

After reviewing carefully the above group of cases one is profoundly impressed with the fact that many subjects wait until the fatal moment before presenting themselves for examination and observation. One must keep in mind that the proximal lesion for a considerable period may be accompanied by vague symptoms of indigestion such as gas, mild intestinal distress, slight loss of weight, diarrhea and constipation. The distal colon may not present any definite physical signs until obstruction or ulceration of the lesion occurs, at which time pus and blood may appear in the stool.

These early symptoms easily may be overlooked by the casual observer—the patient sent on his way with a pill and assured that his disturbance is only an incident in his life. Thus months of valuable time may pass, robbing the patient of the real opportune time to receive proper treatment. The following points should receive consideration in making a diagnosis:

1. A careful history should be taken, making special inquiry into vague digestive symptoms such as diarrhea, constipation and loss of weight.

2. Careful examination of the stool for blood.

3. Roentgen examination of the colon with the aid of a barium enema.

4. Digital as well as proctological examination.

5. Blood count cannot be relied upon except in a few cases located in the proximal colon, which reveal a definite secondary anemia.

6. Late in the course of the disease one is able to palpate a tumor mass.

If the above program is followed many of the patients could be diagnosed early enough so that the surgeon could have a much better chance to reduce his mortality rate.

PROGNOSIS

Carcinoma of the right half of the colon, which is difficult to explain satisfactorily, is of better prognosis than the left half.[13] The cecum has a higher percentage of five year cures and freedom from recurrence than other portions of the bowel.

Age is very important in prognosis. It is well known that a youthful host is at a decided disadvantage in combating malignancy compared to a person in middle or past middle age. This is accounted for on the basis that the older person has developed a sort of immunity or protective element in the body that reacts against the rapid invasion. Further, in the aged, lymphatic system atrophy has occurred and thus metastases are prevented; in the young, the lymph stream presents a wide open channel along which malignant cells may travel from primary foci.

Size of the growth does not enter materially into the prognosis. Large growths on the right side of the colon, due in part to inflammatory reaction, frequently are more promising for relief than are small ones in the sigmoid area, the latter often showing metastases into neighboring glands and the liver (direct extension or blood stream spread). Because of the fecal stream these may ulcerate and bleed earlier and thus be discovered sooner. A tumor, so located, also has a tendency to produce obstruction.

The histologic type of growth encountered is important. The tumor which grows into the lumen of the bowel away from the serosa may be said to be of a lower grade of malignancy, while the smaller growth extending down into the glandular tissue will display a higher type of malignancy and has a tendency to earlier glandular involvement. The time that has elapsed between the discovery of the lesion and the treatment administered is also a very important factor in prognosis.

Inasmuch as most of these cases must be treated surgically, the permeability of the diseased gut with trauma upon handling must be kept in mind. This makes it possible for an exudate which contains virulent micro-organisms to be more easily absorbed. Therefore as little manipulation as possible should be done in exploring under these conditions.[14]

TREATMENT

The treatment of this malady is primarily surgical. Inasmuch as this so thoroughly has been canvassed in the literature, it is not our purpose to discuss the subject at length in this paper. However we wish to call attention to the following points:

A high rate of mortality is recognized as inevitable in dealing with this type of lesion of the colon. It has been recognized for some time that carcinoma in the right half of the colon is more favorable to ultimate cure following resection than it is in the left half. The question of operability is an important one but varies greatly in the hands of different surgeons. The outcome de-

pends upon the taking into consideration the degree of metastases, fixation of the tumor and general condition of the patient. It is commonly agreed by internists and surgeons that from fifty to sixty per cent of the cases are operable at the time of discovery.

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Notes on Diagnosis and Prognosis in Gastric Ulcer: A Clinical Study of Five Hundred Consecutive, Operatively Demonstrated Cases

By

FRANK SMITHIES, Sc.D., M.D.
CHICAGO, ILLINOIS

STATISTICAL studies of large groups of patients affected with a like ailment are frowned upon in certain quarters. While it is granted that in day-by-day diagnosis and treatment individual patients have to be considered, yet, one may not say that, at times, much information of value is not possible from summarizing one's accumulated facts. Grouping them in orderly fashion and thereby securing a proper perspective, the result constitutes a sort of chart pointing main directions but, as naturally could be expected, failing to recognize or indicate each minor curve, obstacle, detour, *impasse*, e.g.—the problem set for solution by the individual patient.

Five hundred operatively demonstrated gastric ulcers are analyzed in this report. One need not emphasize the significance diagnostically and prognostically of discussing proved instances of gastric ulcer: all too often, the literature deals with groups of cases clinically called gastric ulcer. One need not have enormously great experience as a gastroenterologist before he learns that frequently "all signs fail" and when an obstinate "ulcer case" is explored surgically, no ulcer is found by most competent operators: indeed, there is much truth in Deaver's statement that, literally speaking, not more than half the patients being medically treated for gastric ulcer actually are affected with the lesion. In this study instances of *ulcus carcinomatosum* are not included. They have been analyzed elsewhere.

Certain *etiological factors* are of service toward the diagnosis of peptic ulcer. They will be emphasized briefly.

Relative Frequency—Until modern surgery returned definite information respecting the location of peptic ulcers, it was commonly held that gastric ulcer was of more frequent occurrence than was duodenal. Our observations show that in 1,721 instances of proved peptic ulcer, there were 1,225 cases of duodenal and 500 of gastric ulcer, or a proportion of 2.45 to 1.

Age—The greatest number of cases occurred between the ages of forty and fifty. More than three-fourths of the patients were between thirty and sixty years.

Sex—In this series there were 315 males and 185 females, roughly two males to each female. In males the greatest number of ulcers occurred at a decade older than it did in females.

Nationality—American-born furnished 68 per cent. The remaining patients were of European or Canadian extraction.

Occupation—More than 31 per cent of our cases were farmers or people from rural regions and in allied vocations. Practically every other occupation was represented.

Habits—In 145 cases a history of the use of alcohol was obtained. In 26 instances spirits had been used in excess. Smoking or the use of tobacco in any form appeared to be but an accidental factor in ulcer production. To susceptible persons, nicotine or its derivatives appeared to be a factor in increasing gastric irritability, doubtless motor rather than secretory malfunctions.

Dietetic Errors—The frequent occurrence of the disease in America-born farmers (31.4 per cent) is worthy of notice. Overfeeding, careless mastication, hasty swallowing and the tendency to indulge extravagantly in what farmers and food-faddists delight in naming "Nature's Food" would appear to be factors in causing gastric overwork, even if, locally, to the mucosa, mechan-

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ical trauma be discounted. We can find no single dietetic factor of particular significance. Unbalanced rations may condition a certain type of deficiency insofar as theoretic considerations go, but one cannot accuse the dietary of the average American farmer of lacking an abundance of the supposedly "vital" food constituents. In fact, in these stressful years of economic stringency, it is of interest to observe that ulcer incidence has decreased.

Previous Infectious Diseases—Seventeen per cent. of our patients gave a history of having had typhoid fever. Numerous instances of pneumonia, scarlet fever, measles, severe "grippe," tonsillitis, malaria and rheumatism were noted. Twelve patients had had syphilis (2.4 per cent). Frequently it was observed that after an acute infectious disease ulcer symptoms first appeared, or those ulcers already existing, recurred or were aggravated.

Association of Gastric Ulcer With Other Abdominal Pathology—Of the entire series, in 180 patients (36 per cent) who had had previous appendectomy or a laparotomy for ulcer, the appendix was found to be diseased. In 70 instances (14 per cent) cholecystitis or cholelithiasis was found at operation or their previous occurrence had been noted. In other words, of 500 cases of gastric ulcer, affections of the appendix or gall-bladder, generally of inflammatory type, were proved to co-exist at some phase in 250 or 50 per cent. of the series. This observation is of sufficient importance to warrant emphasis from at least four points: (a) The etiological significance of local foci of disease in the appendix and the gall-tract in relation to coincident or subsequent changes in the stomach wall; (b) the prognostic limitations respecting proper stomach functioning following appendectomy, cholecystectomy or cholecystostomy; (c) the failure to relieve dyspepsia by measures directed only to the healing of gastric ulcer in that 50 per cent. of patients who also harbor ailing appendices, gall-bladders or biliary tracts; (d) the advisability of careful anamnesis and abdominal examination of individuals whose only disturbance, symptomatically, appears to be located in the stomach.

In addition to gall-tract and appendix affections, Lane's kink was found five times, pancreatitis thirteen times (2.6 per cent), retroperitoneal sarcoma, carcinoma of the gall-tract, and ureteral stone, each once.

SYMPTOMS

The most striking clinical feature of the disease is comprised in what the word "periodicity" includes. By this we mean that digestive upsets occur intermittently in "spells" or "attacks." Between such periods there is (until stenosis, hemorrhage, perforation, perigastric adhesions or malignant change appears) good gastric health. Of our cases, 360 (69.2 per cent.) fell into this class. These spells of distress frequently bore definite seasonal relation—Spring and Fall being favorites. This is not altogether a valueless observation, if we are to consider bacterial infection as an important etiological factor in the production of gastric ulcer. It will be recalled that in Spring and Fall epidemic infectious ailments are common. At such times, actual infection of a gastric mucosa may take place or a reinfection may occur in a "healed" ulcer or one in process of repair. In all probability the infection or the toxins derived from infection are blood or lymph stream borne. We are not yet convinced by the discussions in the literature—by investigators or by clinicians—that gastric ulcers commonly arise from *primary mucosal* lesions. The evidence that such peptic ulcers are *mural* defects for varying periods *prior* to their exhibiting the *mucosal* ulcer-form lesion, finds much solid support. Indeed, it is our opinion that what clinically is recognized as "ulcer" is but the localized complication of a mural disturbance. Doubtless, in many subjects, similar mural pathologic disturbances in cellular architecture appear which never advance to the mucosa, hence, never produce the ulcer complication which appears in other subjects. Study of the stomach walls of patients dying from various diseases exhibit mural scars and yet peptic ulcer never has appeared.

In a given case, the periodic recurrence of ulcer dyspepsia often happens wholly without regard to medicinal, dietetic or other form of treatment. In this connection, it may be useful to call attention to the fact that various clinicians who have advanced dietetic cures for gastric ulcer (Williams and Donken, Ewald, Weinstein, Boas, Lenhartz, von Leube and a host of others) claim that such "cure" occurs in from 62 per cent. to 70 per cent. of instances. Those figures, it will be recalled, are returned from widely different and frequently opposite modes of therapy. The close approximation of these figures to the incidence of periodicity of manifestation of ulcer shown in this series (69.2 per cent) may be more than a curiously significant coincidence.

It is on account of this periodicity of the disease that usually gastric ulcers give long histories of digestive disturbance. Our records show that more than 52 per cent. of cases had been dyspeptics from five to twenty years before operation. Less than 20 per cent. had been affected for a shorter time than five years. During these intervals, attacks of distress ranged in frequency from one every three to five years to a gastric upset every two or three weeks. In less than 24 per cent. was the ailment continuous. The individual attacks varied in severity. The gastric health in the interim generally was excellent. Weight was not infrequently lost during the "spells," but rapidly gained so soon as abdominal distress subsided. The average weight loss was 18.2 pounds. There were instances where as much as 65 pounds were lost within a few months, or 28 pounds, in rather more than three weeks. The weight loss,

even if strikingly rapid, rarely was associated with the cachexia usually accompanying that in malignant disease. The systemic toxic evidences were lacking. Weight loss only was progressive so long as gastric symptoms existed in a given "spell." The gain when an attack passed often was astonishingly rapid. Night pain with loss of sleep, constant abdominal distress with dread of aggravating such by eating, or caution in the quantity and the kind of diet on account of recent hemorrhage were important factors in the production of weight loss.

Even without gross hemorrhage, *anemia* not uncommonly went hand in hand with intermittent decrease in weight. The hemoglobin in our series averaged approximately 76 per cent. The red cell count was above 4,000,000 in eight of ten instances where hemorrhage recently had not occurred. The white count in non-perforating ulcers rarely was higher than 11,000 cells.

As we have stated, the gastric ulcer patient generally enjoys good health between attacks. This is maintained in these intervals so long as such complications as pyloric stenosis, perforation, perigastritis or hour-glass contraction do not develop. In these events the ailment becomes a continuous dyspepsia in contrast to the previous periodically recurring affection, with stages of aggravation.

The symptomatology in the attacks largely is covered by observation of epigastric pain, vomiting, hemorrhage, weight loss, weakness and anemia. The signs of the ailment generally consist in evidences of abdominal tenderness, alterations in gastric secretion and emptying power, phenomena elicited upon X-ray examination and unusual findings in the stools. A brief consideration of these departures from the normal is offered.

1—*Pain*—In 98 per cent. of the cases comprising our series, some form of gastric distress was noted.

Character of Abdominal Discomfort—This was variously styled "vague discomfort," "burning feeling," "gnawing," "dull ache," or "soreness." In 19.6 per cent. colicky attacks were observed. Such pains variously were described as "tearing," "doubling up," "cramps," or "piercing." They were so severe as to require opiates in 9.4 per cent.

Location, Symptomatically, of Abdominal Discomfort—In nearly four of five instances pain was generally epigastric, without definite point of intensity. In 12.2 per cent., the area of maximum distress was toward the right rib margin. Fifty-two patients had sternal pain; 31 complained of general abdominal soreness, while eight had distress in the "small of the back."

Transmission of Pain—In about one of three cases there was no transmission of distress. In the order of frequency, referred pain was noted in the right scapular region, the right rib edge, the infranavel region, between the scapulae, at the sternum, throat and nipples.

Time of Occurrence of Pain—In 415 instances (83 per cent.) pain or distress had definite relation to food ingestion. It was recorded that in more than three of four cases pain occurred within four hours following the taking of food. In uncomplicated ulcers, pain usually came on sooner after a light meal than after a large one, i. e. pain-or distress-relief, by food intake, was not so long maintained.

Relation of Time of Manifestation of Abdominal Distress to the Location of Ulcer—Irrespective of the location of the ulcer it was shown that nearly 80 per cent. of instances had distress within four hours after eating; nearly 50 per cent discomfort within three hours after food; more than 44 per cent. of lesser curve ulcers had pain one to three hours *post cibo;* nearly two-thirds of the ulcers located near the cardia had maximum distress within two hours following food intake, and two of five within one hour afterwards.

Pain Controls—Except in the acute accidents of the disease or when pyloric obstruction or "hour-glass" contraction occurred, distress in gastric ulcer most commonly is relieved by limitation of the amount or alteration in the character of ingested food (diet), the taking of food when distress is most marked ("food-ease"), the so-called "neutralization" of acid by alkalies or by emptying the stomach (vomiting, lavage). As has been mentioned, opiates are not infrequently required. When such is the case, usually one is dealing with the perforating type of ulcer or a lesion which has progressed outward to the stomach's serous covering.

The observation of relief of gastric distress by food ingestion is of prime importance in diagnosis of uncomplicated peptic ulcer. If its history *constantly* is obtained, it is practically pathognomonic in three of five cases. While patients, on casual questioning, frequently state that food distresses them, yet careful inquiry will elicit the fact that food does not at once cause discomfort, but that such comes on from one to four hours following eating. If the gastric lumen is not obstructed (hour-glass contraction) or if the pyloric channel remains patent, our observation is that the duration of food relief of pain bears direct proportion to the size and character of the meal taken, i. e. the larger the meal the longer the period of pain relief. Liquid food-relief is not infrequently more prompt than is that obtained by solids. The dread of pain following food intake often leads to an anticipatory attitude on the part of the patient. This state of mind appears to exert a not altogether negligible influence towards the production of uncomfortable gastric spasms. That this is so, readily is shown by the change occurring in pain time and pain intensity following the administration of atropine or bromides. A game of golf, cards or football, an absorbing yarn, a hike, a "remedy" supposedly possessed of rare

properties or even the ministration of a personality-potent osteopath or a christian science "healer" very often is followed by similar beneficial effects.

2—*Vomiting (Frequency)*—This is an important and often an annoying symptom. Of the 500 cases of gastric ulcer making up this series, 390 patients (74 per cent.) gave history of vomiting. There were 164 instances of non-obstructing ulcer; of this number 104 or 63 per cent vomited. There were 336 cases where some degree of pyloric obstruction or malformation of another part of stomach obtained. Of this group, 286 cases (85 per cent.) vomited sour fluid, food or both. In all instances, vomiting depended largely on the character of food intake. Commonly, solid food more regularly produced vomiting than did liquid. At times of acute exacerbation of distress, the factor of gastric or pyloric spasm proved an important cause of emesis. At such periods, frequently even non-obstructing ulcers gave vomit pictures similar to those where there was anatomic hindrance to the onward progress of food.

"Delayed" vomiting, that is, vomiting of food which has lain in the stomach for from eight hours to several days, was exhibited by 22 per cent. of the ulcers forming the non-obstructing group and by 68 per cent. of those where ulcer scar caused some type of lumen stenosis. Cases exhibiting "delayed" vomiting showed varying degrees of gastric dilatation in nearly eight of ten instances. Often they had been treated for such on the strange supposition that dilatation of the stomach is, itself, a *disease;* such condition is of extreme rarity in the presence of gastric ulcer.

Of the 390 patients who vomited, 172 (44 per cent.) vomited regularly. Two hundred three cases (52 per cent.) vomited occasionally, generally when attacks of abdominal distress occurred. When pyloric stenosis was present in various grades, vomiting was regular in 262 such cases (78 per cent.). In high-strung, apprehensive patients, powerful gastro-spasms often are responsible for air aspiration from the oesophagus ("air swallowing"). This presence of air in the stomach not rarely causes not alone vomiting but also the appearance of epigastric pain or aggravation of pain otherwise mild.

While vomiting is most common in ulcers involving the pylorus and the pyloric half of the lesser curvature, yet vomiting may occur wholly independent of the location of the gastric ulcer.

Nausea without vomit was a distressing symptom in 46 cases of this series. Pyrosis, eructations or "water-brash" was noted in 410 cases (82 per cent.). Very frequently these were both annoying and persistent and often led to overmedication or the pernicious use of stomach tubes. One should not forget that, often enough, the vigorous exhibition of alkalies is responsible for increased secretion of gastric acid and what, perhaps, is of more serious consequence, alterations in blood chemistry, renal damage and certain rather obscure central nervous system anomalies.

3—*Hemorrhage*—History of gross bleeding, either hematemesis or melena, was obtained in 182 cases (36.4 per cent). Thus it is shown that, while such sign, when taken into consideration with other clinical facts, practically is pathognomonic, yet only one of three cases exhibits it. Hence, nearly twice as many cases of gastric ulcer must be diagnosed by signs and symptoms exclusive of gross bleeding.

Of 182 cases which had bled, 148 patients (80.2 per cent) had shown hematemesis with or without melena. Thirty-two instances (17.1 per cent) where melena alone had occurred were noted. Fifty-eight patients (31.8 per cent) had shown both melena and hematemesis.

Severity of Hemorrhage—The minimum number of hemorrhages was one. Several instances where from ten to fifteen hemorrhages had occurred were recorded. Of those bleeding, one of four suffered no inconvenience. In about one of three, faintness with symptoms of shock was described. Approximately two of five actually fainted. While a first, gross hemorrhage rarely is serious or fatal, yet it must be emphasized that instances of gastric ulcer associated with mild clinical manifestations, suddenly may exhibit bleeding so copious or so uncontrollable that *exitus* follows before adequate treatment is possible.

Relation of Ulcer Location to Hemorrhage—Hematemesis is of more frequent incidence than is melena, wholly irrespective of the place occupied in the stomach wall by the peptic ulcer. It is interesting to observe, however, that melena *only* may occur with ulcers located on the lesser curve or in the *pars media*. In general, however, melena alone means that the ulcer is situated well toward the pylorus. On the other hand, hematemesis alone may occur with an ulcer located in any position.

Relation of Hemorrhage Incidence to the Character of Ulcer—Our operative and post-mortem examinations of ulcers reveal that while ulcers in all grade of chronicity may bleed, yet approximately three of five exhibiting this accident show some grade of perforation, protected or otherwise. Ulcers, which once have bled grossly, exhibit a tendency to bleed again; the interval between hemorrhages may be as brief as a few days or weeks or as widely separated as ten to twenty years. In the interim, digestive health may be excellent. Hemorrhages may appear with no gastric prodromata. Therefore, once an ulcer has bled grossly, the physician should be extremely reticent with respect advancing a too-optimistic prognosis or in holding that clinical cessation of ulcer-dyspepsia indicates final histologic repair at the ulcer site. Our studies would appear to suggest that gastric ulcers which bleed grossly form the group most likely to exhibit acute, *often fatal,* perforation.

THE SIGNS IN GASTRIC ULCER

(a)—*Abdominal Tenderness*—In our series some degree of abdominal tenderness was demonstrable in 465 cases (93 per cent). While with gastric ulcer, the epigastrium, generally, is tender to deep palpation, in more than three of four of the cases comprising this study the area of maximum epigastric tenderness was at or to the right of the midline. In 57 instances (11.4 per cent) the greatest discomfort on palpation was elicited to the left of the midline. In 45 cases (9 per cent) there was special tenderness in the "pit", irrespective of general epigastric sensitiveness. Tender and palpable "ridges" were demonstrated nine times (1.8 per cent).

Relation of Areas of Abdominal Tenderness to Locations of Ulcers Demonstrated at Operation—Our laparotomy statistics show that nearly four of five gastric ulcers were located at the pylorus or in the region distal to the pyloric half of the *pars media*. We have shown above that more than 75 per cent of patients exhibited epigastric tenderness in the right upper, abdominal quadrant. It would seem that, when taken into consideration with other observations, points of abdominal tenderness are of certain practical value towards locating gastric ulcers. It should be emphasized strongly, however, that similar areas of epigastric distress can, not infrequently, be demonstrated in pyloric spasm due to disease of the duodenum, gall bladder or the appendix.

(b)—*Alterations in Gastric Secretion and Emptying Power—Test Meal Findings*—As we have mentioned, 336 of our cases (67 per cent) showed some evidences of retained contents when, following a full meal of mixed food stuffs, the stomach was emptied after a twelve-hour interval. In 164 instances (32.8 per cent) emptying time was not interfered with. We determined this deficiency in emptying power by the simple procedure of taking the patient off "diet", administering a mixed meal containing, in part, boiled rice and twenty raw raisins, and then searching for food remains at gastric lavage after twelve hours. From the personal examination of more than 18,000 stomach extracts, I have concluded that only the *persistent* demonstration of food retained in a stomach longer than *ten hours* has definite significance towards the proof that the gastric lumen is not freely patent. Retention of food for from *four to eight-hour* periods readily is demonstrated, *intermittently*, where pyloric or gastro-spasm exists with hyperacidity associated with vagotonia, gall-bladder disease, duodenal irritation or appendicitis or from malnutrition, fatigue or central nervous system dysfunction. The persistent finding of test-food remnants (raisin, skins or coarse food particles) after a twelve-hour interval is an indication of organic obstruction; such finding indicates that a mechanical cause for retention is present and that the obstruction calls for relief by mechanical, i. e. surgical procedures. Dilatation of the stomach generally co-exists in such cases, but such is a secondary, compensatory change. Of course, on "baby food" patients with high grades of stenosis may live, even gain weight and be comfortable. In such circumstances, a regular meal—too often called an "indiscretion or lapse" in diet—precipitates a digestive upset, usually accompanied by vomiting. Few patients care to live for years on pap; hence, if apart from gastric stenoses, otherwise they are sound, it would seem that from the standpoint of good fellowship and good sportsmanship alone, their stenoses should be relieved surgically and promptly, particularly since operations giving such relief are simple and accompanied by so low a mortality.

Acidity of Gastric Extracts—In the retention cases, the average free HCl was 56.4; the average total acidity, 74.2, and the combined acids and salts, 17.8.

In non-retention gastric ulcers the free HCl averaged 40.5; the total acidity, 52.4, and the combined acidity, 11.6.

It was observed that the highest gastric acidities uniformly were determined in acute and subacute perforating ulcer; that in simple, chronic gastric ulcer the figures closely resembled those returned from cases of *ulcus carcinomatosum* and of chronic gastritis. Where recent bleeding had occurred, the free HCl averaged 35, the total acidity 48, and the combined acid and acid salts, 13.5. These figures very closely resemble those of early malignancy or of malignant ulcer. In chronic ulcer of benign type, with retention, there is an increase both in free HCl and total acidity. This is in sharp contrast to instances of retention developing in malignant ulcer, where, as stenosis occurs, free HCl progressively is lowered, while total acidity correspondingly increases.

Blood, macroscopically or by the benzidin test was noted in 39 per cent of gastric extracts. Frequently, such blood came from tube manipulation and had no apparent relation to the activity or quiescence of the peptic ulcer. Very often patients were lavaged within forty-eight hours of severe hemorrhages without blood being noticed in the removed test meals.

While we are considering the incidence of blood in gastric extracts, it might be useful to call attention to the fact that chronic gastric ulcers bleed only intermittently. To anyone who has observed the pathological alteration occurring at a point where an ulcer is situated, the reason for this intermittent bleeding is evident. An ulcer cannot exist for very long without a tissue-reaction occurring at its edges. This tissue reaction is at first the hyperplasia of repair. Eventually it results in the production of scar tissue. Unless the ulcer progresses very rapidly and proteolysis causes destruction of vessels of fair size, gross hemorrhage rarely occurs. The bases of most ulcers are clean. This pathological explanation is sufficient to warn one not too constantly to expect blood either in gastric extracts or stools when

ulcer deformity is demonstrated by roentgen studies.

On account of this intermittent bleeding of gastric ulcer, so-called "raw granulating surfaces" occur only at times of activity of the process. Thus, it is seen that such technical manoeuvre as the localization of an ulcer or the determination of its existence by means of the "string test" has but limited diagnostic value. We have made observations with the "string test" upon 318 cases of gastric ulcer. In only seven instances were we able to observe unqualifiedly definite blood stains upon the test string. These stains practically were always at a distance approximating that where theoretically we located the pylorus. Knowing the pathological fact that two-thirds of all ulcers are located in the pyloric third of the stomach, it is not difficult to prognose, when a blood stain occurs upon a string, that a suspected ulcer will be in the pyloric region. One can do this quite well without the use of a test string when he knows statistics of ulcer location and knows, also, that gastric ulcer is present. It should be emphasized, also, with respect to the "string test" that gastric and jejunal peristalsis carry the string forward in the straightest possible line. From experience in passing stiff duodenal catheters upon thread guides, we have convinced ourselves that after a string has been in the stomach or the jejunum for six hours, it hugs closely the lesser curvature and the superior surface of the pylorus. Knowing, as we do, the location, the variation and the character of gastric ulcers, readily one can see how many strings actually never can come into contact with ulcer surfaces, particularly if the stomach lies open as a sac: ulcers not located along the lesser curvature or in the pyloric section of the antrum remain away from those parts reached by a string swallowed for "diagnostic" purposes. In but few active clinics does one see employed the "string test" for the diagnosis of or to determine the histologic status of gastric ulcer, even though, in textbooks carrying relatively modern dates, considerable space is given to this manoeuvre. In cases where there is pyloric stenosis, the diagnostic value of the "test string" is almost nil, for the simple fact that the string frequently does not reach the ulcer.

Blood in the Stools—As we have stated above, the intermittency of bleeding in gastric ulcer warns one never to delay diagnosis of the lesion until the appearance of "occult blood" is proved in the stool. In our cases, rather more than 31 per cent gave positive benzidin reactions in the properly prepared stool. Unless the stool is properly prepared, one may obtain positive chemical tests for blood in specimens from the majority of suspected ulcers examined. Such reaction comes usually from material ingested as food. To eliminate this error, we have found it necessary to place our patients, after catharsis, upon meat-free diet for at least forty-eight hours, and then upon absolute milk or cereal gruel diet the twenty-four hours preceding the time for the collection of the stools. If this technique is adhered to, the chemical finding of blood in a patient, *with an ulcer history*, then is of significance with regard to telling of the *activity* of the ulcer more than as a diagnostic aid in telling us that an ulcer is present. This information particularly is useful in cases where one suspects that malignant change has taken place in an ulcer edge. Malignant ulcers are apt to break down quickly and, in such cases, chemical tests for blood in the stools are commonly positive. Of prime prognostic as well as diagnostic significance, is the *constant* observation of occult blood in the stools or the gastric contents of an ulcer-patient in whom, previously, one has been able to demonstrate positive chemical tests only *at intervals*. In such circumstances, one must consider that the gastric ulcer has become malignant and advise surgical intervention.

X-ray Evidence of Gastric Ulcer—Our observations are based upon a personal study of the reports of nearly 3,700 examinations of patients with gastric symptoms. All patients were examined both by the fluoroscopic and the plate or film methods. We believe that the internist personally should fluoroscope his patient or at least should be present at such examination. Also, he should make a practice of studying and comparing films with the chemical, physical and operative findings and should review history data in the light of what roentgenograms reveal. In this roentgen series there were 326 proved instances of gastric ulcer.

It is well to state that in uncomplicated gastric ulcer, the X-ray evidences as shown by the film method are largely accidental or inferential. By uncomplicated ulcer I mean ulcer in which pyloric stenosis has not occurred, where types of hour-glass contraction have not taken place, where malformation of the stomach outline by excess of scar tissue has not ensued, where perforation is absent or crater ulcer does not exist. When it is recalled that the X-ray film in gastric work is but a silhouette of the bismuth-filled stomach at one instant of its exposure and with the patient in various positions during the exposures, readily it is seen why X-ray films do not locate all ulcers. Further, when we realize that less than 35 per cent of chronic gastric ulcers are of the complicated type, it is not difficult to appreciate that many ulcers must escape recognition in the X-ray film. The most important evidence returned by the X-ray film is the demonstration of various types of stenosis, indication of the size of the stomach, differentiation between simple and malignant ulcer and a gross carcinoma, the relation of the stomach to adjacent viscera and the proof that the lesion actually is in the stomach and not in the duodenum or in another viscus. Many of these facts can be determined less expensively by the simple, clinical methods such as we have al-

ready outlined: by careful history taking and intelligent scrutiny of data derived from physical examination.

It is safe to say that, while in a given case, it is extremely desirable for purposes of record to have X-ray films made of the bismuth-filled stomach, the X-ray examination, by means of the fluoroscopic screen gives the greatest amount of information in far shorter time and at less expense to the patient. One method admirably supplements the other type of examination, but it is difficult to see, after any amount of clinical experience, how the film method alone can satisfy the clinical needs. It is an injustice to the roentgenologist to expect him to bear the main burden in diagnosis and prognosis and to suggest therapy: a course, however, which all too commonly is followed by physicians, particularly physicians in general practice. The roentgenologist is a consultant for the internist and can give special information valuable along particular lines: he should not be expected to do the entire job. The fluoroscope itself is not infallible in determining the presence or absence of gastric ulcer. Its range of activity is greater than that covered by the film method, because, within a few minutes, one can see the stomach in a great variety of phases of activity and can add to this visualization the changes in gastric action that may be brought about during abdominal palpation and with the subject in different positions. As results of these added advantages, one not infrequently proves the existence of an ulcer where the film had been negative or shows that what appeared pathognomonic of uncomplicated ulcer in the plate is but an artifact or is due to causes, extra-gastric in origin. This is particularly the case when the patient is fluoroscoped at several sittings before and after the use of atropine or belladonna to relax pyloric or gastric spasm. With the employment of the new "compression" technique and through the ingenious contrivances which permit serial X-ray exposures while the screening is progressing, many gastric ulcers otherwise impossible to demonstrate by ordinary methods, become provable.

From the above it must not be understood that in our opinion the X-ray film examination of patients is of limited value. On the contrary, we consider that facts of great importance often are obtained by the X-ray technique. Clinically, we have come to regard X-ray examinations as having the same relative worth in gastric ulcer diagnosis as has a differential blood count in cases of anemia. While at times nothing is added to the clinical picture, there are occasions when the diagnosis actually is *given* by such examination. Certainly, it is to be deplored that unproved and wild statements have been made regarding the absolute diagnostic worth of the X-ray examination of the bismuth-filled stomach. The procedure is so largely a mechanical one that no hard-and-fast rules can be laid down with respect to diagnostic signs as returned by its application. The interpretation of what is seen in the film or felt and seen at the fluoroscopic examination is highly individual: an experienced clinician-operator is capable of returning diagnostic information of far greater worth than is an operator whose dependence is entirely upon gross anomalies exhibited by films. Added danger from the use of these mechanical procedures, clinically, is to be found in the fact that in the novelty and the perfection of new mechanical devices, clinical cerebration tends to decline, and simple, well-proved methods of diagnosis are forgotten. It is our custom to *terminate* the examination of a gastric case with the X-ray examination. In fully 85 per cent of our cases the diagnosis has been well established without the X-ray findings. However, a not negligible advantage of X-ray procedures is the demonstration of the exact location of the ulcer, its size, pathologic character, relation to adjacent organs, effect upon gastric filling and emptying and, a feature but recently stressed, the changes which take place during the exhibition of therapeutic regimens. Finally, where a gastric ulcer bleeds *constantly* (as shown by chemical tests for blood in the gastric contents or the stools), should that ulcer exceed 2 cm. in diameter, in all probability, one is dealing with a lesion undergoing malignant change. Especially is this so if the ulcer lies in the pyloric fourth of the stomach and when careful history-taking brings out the facts that the patient's family has had cancer in the blood relatives during two or three past generations.

PROGNOSIS IN GASTRIC ULCER

The clinical course of any gastric ulcer is highly individual. While it is true that we have undoubted histological proof that many ulcers heal, we have yet no means of determining, clinically, in a given case, whether or not such ulcer will heal in its acute stage, will exhibit benign chronicity or will become the basis of a future cancer. It has been shown, however, from the mass of data, carefully studied, which has accumulated during the past decade, that many gastric erosions and simple ulcers have a "natural" tendency toward healing. This event not uncommonly occurs wholly irrespective of the clinical type of treatment carried out. Also it is a commonly observed fact that a given ulcer will tend to chronicity and recurrence in spite of all known methods of therapy. In such cases, prognosis is dependent largely upon intensely individualized pathology and factors, of which we have but scant knowledge, concerned with ulcer production. If the process continues benign, the resultant condition demanding treatment largely is accidental. Pyloric stenosis with gastric dilatation, hourglass contraction, perforation involving other viscera or malignant degeneration may occur without regard to, in fact, in spite of, clinical care. Each patient is a law unto himself. In many instances of chronic gastric ulcer, the ulcer itself

heals, but in the healing, complications occur which may require surgical treatment.

We have no known means of telling, clinically, in any case of gastric ulcer, and particularly in those gastric ulcers which run a chronic course, what the ultimate outcome will be. The life history of the affection seems to depend upon unknown factors. It is coming to be more generally recognized, however, that gastric ulcers of the chronic type which have a tendency to frequent recurrences may terminate in malignancy. Particularly is this so when the hereditary factor of cancer in general, and gastric cancer in particular, is outstanding. As Macklin has pointed out, not sufficient care is exercised, during history-taking, towards a searching and intelligent enquiry into from what ailments the ulcer subject's blood relatives actually died. Certainly, clinicians who neglect such enquiry as a regular part of history-taking, are missing important facts with respect the case at hand and are failing to contribute information toward the subject of "cancer heredity" in general. At present, we do not know how often malignant transition takes place. It should not be understood that all chronic gastric ulcers become malignant. Possibly not more than 5 per cent exhibit that complication. However, it should be firmly emphasized that, in a given chronic gastric ulcer, we have at present no means at our command which enable us to tell which chronic ulcer is destined to pursue a benign course and which will become malignant unless we secure facts from the family history. The future course of chronic gastric ulcer is dependent wholly upon the character of the tissue reaction to hyperplasia. When the clinical pathologist not uncommonly is unable to differentiate between benign and malignant hyperplasia, it is very difficult to see how the internist, prior to operation, is to be expected to prognose the future course of any gastric ulcer unless, perhaps, he deals with a previously periodically active ulcer which later becomes constantly active and the roentgen studies demonstrate an ulcer whose diameter exceeds 2 cm. Certainly, from our studies of gastric cancer, it would seem, however, that more cases of this affection developed from previous "benign" ulcer than generally has been recognized.

In a former study* we analyzed 566 consecutive cases of operatively and pathologically proved *gastric cancer*. This study showed that the sex ration in these cases approximately was that of chronic gastric ulcer; that the average history of the affection, before evident malignancy occurred, extended over 11.4 years in two of three cases; that the supervening period of evident malignancy averaged 6.1 months; that but one of three cases of gastric cancer had no previous dyspeptic history; of this group the whole course averaged 7.1 months; that of the entire series, in 92 cases where gross hemorrhage had been noted, the bleeding occurred in nearly 63 per cent in those with previous "ulcer history" and that of the whole number bleeding, 52 per cent had bled two years prior to their coming under observation; that of those who bled within the two-year period, 77.5 per cent of the cases fell into that group with "ulcer history" previous to a period of evident malignancy; that in but 55.4 per cent was free HCl acid absent from the gastric extracts and that in 31.5 per cent it ranged between 20 and 50. Certainly, when one analyzes any great group of operatively proved instances of *gastric cancer*, he cannot fail to be impressed by the evidence that not more than one-third of the cases of gastric cancer appear in subjects who previously had no dyspeptic history; and the history of such dyspepsia is that commonly interpreted as indicating the presence of gastric ulcer. Ulcer prognosis cannot disregard these facts. Gastric ulcers which recur frequently should be removed surgically before they have opportunity of becoming cancers.

Apart from considerations of malignancy and the limitations to free feeding imposed upon gastric ulcer hosts, the affection is not one especially to be dreaded. In not more than 18 per cent of patients do such complications as stenosis, perforation, peri-gastritis, etc., develop. If we include the possibilities of malignant change, the total of serious complications in gastric ulcer approximates 25 per cent of all instances. In other words, 75 per cent of gastric ulcer patients do not die from their ulcers. Periodically they are dyspeptics and, hence, may suffer certain economic handicaps but they need not be overly fearful of death or of complications requiring surgery. Doubtless, if patients were widely acquainted with this information, their ulcers would give less discomfort; they might heal quicker if the nervous element were removed. The recent observations of Rivers and Dry on this aspect of peptic ulcer and peptic ulcer treatment are particularly pertinent. Frankly, we consider that it is the ethical duty of every trained, experienced gastro-enterologist constantly to endeavor to relieve gastric ulcer patients of some of the dread and apprehension which, too often, overwhelm them once they have been acquainted with the cause of their dyspepsia. Watchful care is due these patients but in the course of such care aid to relief or cure may be derived from optimism and assurance. Very commonly, to the patient, a diagnosis of gastric ulcer implies ultimate gastric cancer. It is not to our credit that frequently physicians do nothing to counteract such impression or lessen the dread of such termination.

*Smithies: The Relation of Gastric Ulcer to Gastric Cancer. (Jour. Am. Med. Assoc., 1913, p. 1703, November 15.)

An Unusual Right Diaphragmatic Hernia*

By

WILLIAM C. BOECK, Ph.D., M.D., F.A.C.P.

and

WELLS C. COOK, M.D.

LOS ANGELES, CALIFORNIA

INSTANCES of right diaphragmatic hernia are exceedingly rare. Geyman[1] reported the large series of Eppinger in which 626 cases represented left diaphragmatic hernia, while only eight were right diaphragmatic hernia. In another series of Thomas, reported by Geyman, eight were right and 282 were left. In 1924, Carman and Fineman,[2] of the Mayo Clinic, reported a series of 17 cases, of which 14 were left and three were right.

The clinical diagnosis of diaphragmatic hernia may be suspected when the patient gives a history of receiving a sudden blow in the abdomen, usually in the upper abdomen, following which often there are pain and shock with collapse. Later, the patient has discomfort after eating with a sense of pressure in the right or left lower chest, depending on the site of the hernia. This discomfort is increased upon lying down and somewhat relieved by standing. Small herniae are as apt to give as much discomfort as are large ones, sometimes more, since the latter may offer little obstruction to the passage of food. In left-sided diaphragmatic hernia, there may be additional symptoms such as palpitation from pressure on the heart, this being worse when the person lies on his right side; upon exertion there may be some dyspnoea and shortness of breath. These latter symptoms often lead the examiner to suspect either cardiac or pulmonary disease instead of diaphragmatic hernia.

In right diaphragmatic hernia, the pressure-symptoms in the right side of the chest may follow eating and exertion, usually with dyspnoea and shortness of breath, and sometimes pain. Often the patient hears the gurgling rush of fluid high in his chest as compared with the uninvolved side. In these cases of right-sided hernia, the subject cannot sleep well on his left side, because of palpitation and the sensation of pressure produced by the herniated viscera lying against the pericardium.

From a roentgen viewpoint, the diagnosis of *left* diaphragmatic hernia is comparatively simple. The fluoroscopic examination or the X-ray films usually show the stomach with its tell-tale gas bubble and often the haustrated gas-filled loops of the colon, lying up in the thorax.

On the other hand, the roentgen diagnosis of *right* diaphragmatic hernia offers a certain problem in differential diagnosis. In the films, the lower half of the chest may appear opaque and so suggest pleural effusion, atelectasis or an old thickened pleura. Especially is this true when there is no gas present in the herniated viscera. In the fluoroscope, however, it is not such a puzzling problem inasmuch as the air shadows in the lung parenchyma often are visible about the sides of the contained viscera. When the stomach alone is present in the hernia, the tell-tale gas bubble seldom is seen because it remains in the fundus when the person is in the upright position. When a loop of the transverse colon is present, and gas is contained within it, the bowel is readily identified at the fluoroscopic examination.

Unfortunately, in many of these cases a fluoroscopic examination is not available to determine the cause of the opacity in the lower chest as shown in films, and the result is that a diagnosis of right pleural effusion often is made. This diagnosis then leads to repeated thoracentesis. Such confusion, occurring in a child, was reported by Truesdale.[3] Thoracentesis produced the flow of a milky fluid through the needle because the child had ingested milk previously and the needle had entered the stomach. Our own case, reported below, also illustrates this point. Supposing the opacity on the right lower chest to be due to fluid, one physician sought to tap it, but only blood was obtained and the procedure was interrupted. On still another occasion, another physician, falling into the same error, obtained a turbid, watery fluid, but no observation was made to determine whether or no the roentgen opacity in the chest diminished in size. Now we know that this physisian obtained gastric fluid.

CASE REPORT

The following is a brief history of a patient in whom right, diaphragmatic hernia was found.

Case J. E.—Age 41, male, white, unmarried; occupation, automobile racer and salesman. The family history was not important. The patient had the usual childhood diseases, had suffered a skull fracture in 1921 with skin burns following an auto-racing accident.

He was seen by one of us (W.C.) on January 17, 1934, at which time he complained of pain in the right chest on exertion, shortness of breath, palpitation on lying on his left side and pressure in the lower right chest after eating and on lying down.

The present illness had its onset in June, 1927, following an accident while piloting a car in the Memorial Day races at the Indianapolis Speedway. When the accident occurred, the patient was thrown violently against the steering wheel. He became unconscious; on awakening

*From the Los Angeles Medical Group and Clinic.
Submitted October 22, 1934.



Fig. 1. Barium-filled stomach and colon in right thorax. *F.* (fundus), *Pyl.* (pylorus), *D.C.* (duodenal cap), *C.* (colon).

he suffered much pain in the right chest and was removed to a hospital. After examination, it was reported that a *couple of ribs* had been fractured on the right side and fluid was present in the right chest. Pneumonia followed but the patient recovered. He stated that the fluid remained in his chest for the next two years, but, in 1930, a physician obtained only blood on performing a thoracentesis. His symptoms continued and, in 1931, another thoracentosis was *done*; on this occasion a turbid, watery fluid was obtained. No improvement was noted in his symptoms. The patient could not resume his auto racing because the exertion caused pain in his right chest, associated with shortness of breath. He could not sleep on his left side as that position caused palpitation and a *feeling* of pressure about his heart. He had experienced pressure in his right chest on lying down and after eating.

Physical examination (January 17, 1934, at 4:00 p.m.)—height 5 feet 9 inches, weight 161 lbs., temperature 98.6 degrees, pulse 76, respiration 18. Patient presented the appearance of a well-developed and well-nourished man, experiencing no apparent pain or discomfort. The scalp was clear; there was a recession of the hair over the temples. The eyes, nose, and ears essentially were negative. There was no adenopathy or palpable thyroid. The *chest* examination revealed no diaphragm excursion and *percussion* dullness over lower half of the right chest with absence of breath sounds; râles were absent. *Heart*—left border dullness was at the nipple line; the sounds were regular and no murmurs were heard. The blood pressure was 118 72. *Abdomen*—scaphoid with moderate subcutaneous fat. Palpation elicited no tenderness or masses. The liver edge could not be felt, nor could the spleen. Genito-urinary examination and extremities essentially were negative.

The patient then was referred to one of us (W.C.B.) for X-ray films of chest and a fluoroscopic examination. The *X-ray* film revealed an area of opacity occupying the right chest extending from the level of the fourth rib anteriorly downward. The shadow was uniformly dense throughout and suggested fluid. The *fluoroscopic examination* showed small gas collections within this opaque area; a diaphragmatic hernia was diagnosed. The patient was then given a drink of barium sulfate suspension. The barium was observed to pass into the pylorus which then was seen to be located in the opaque area of the right chest. This demonstration was facilitated by having the patient lean to the right. A gas bubble remained and its presence signified that, in addition to the pyloric half of the stomach, the colon also was included in the hernial area intruding into chest cavity.

Films were taken at once and again on the following morning. These films (Figs. 1 and 2) reveal the presence of the terminal half of the stomach and the duodenum as well as a loop of the transverse colon within the right chest. Furthermore, soft tissue shadows indicated the presence of the right lobe of the liver in the chest and extending upward to the level of the fourth rib (Fig. 2). No leaf of the right diaphragm could be demonstrated. The left diaphragmatic leaf was intact; the fundus of the stomach lay just below it; adjacent to it was seen the shadow of the spleen and kidney (Fig. 2).

The *roentgen diagnosis* was a large, right diaphragmatic hernia associated with the pyloric-antral portion of the stomach, a loop of transverse colon and the right lobe of the liver in the hernia and lying within the thoracic cage.

Operation—Subsequently the patient decided to seek surgical aid at the Mayo Clinic. On April 7, 1934, Doctor S. W. Harrington operated. We are indebted to him for supplying us with the details of the operation. We quote from his letter:

"His case has, indeed, been a very interesting one as it is quite unusual to have a traumatic hernia in the right diaphragm with practically the entire liver in the thorax. At the time of operation on April 7, we found a huge opening in the right diaphragm extending diagonally across from the anteromedial portion to the posterolateral portion of the diaphragm. Practically the entire stomach,

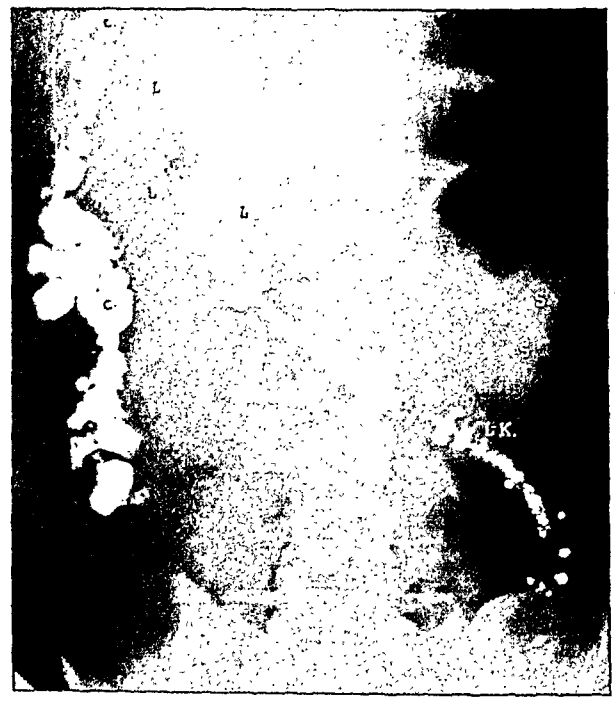


Fig. 2. Barium-filled colon lying in right thorax. *C.* (colon), *L.* (liver in thorax), *F.* (fundus with gas bubble), *S.* (spleen), *L.K.* (left kidney).

all of the transverse colon, hepatic flexure of the colon and greater omentum, the entire right lobe of the liver and the gall bladder had herniated into the right thoracic cavity.

"We were unable to separate the liver from its attachment in the thorax through this incision, as it was adherent to the pericardium, the great vessels, the lung and chest wall. After separating the remaining herniated viscera and replacing them in the abdomen, the abdominal incision was closed and a thoracotomy was done, resecting portions of the eighth and ninth ribs. The liver was then separated and replaced in the abdomen and the opening in the diaphragm was closed. A satisfactory closure was made possible by a phrenic nerve interruption which permitted relaxation of the muscles of the diaphragm. The pleural cavity was then closed and a blood transfusion was given before the patient left the operating table."

Subsequently the patient made a satisfactory convalescence although it was complicated by a post-operative empyema. According to Dr. Harrington, further surgery may be necessary in an attempt to collapse the remaining cavity produced by the failure of the middle and lower lobes of the right lung to expand.

This case is unusual from several angles. It was remarkable that the condition remained undiagnosed for almost seven years. Because of the mistaken diagnoses, two needless thoracenteses were done, either of which might have proved fatal if peritonitis had followed. Finally, the lesion was uncommon because of its right-sided position and the magnitude of the hernia which permitted displacement of the liver, the gall bladder, one-half of the stomach and the transverse colon to a position in the right thorax in which situation they became adherent to the pericardium and the great vessels.

It is for the reasons specified and because the patient successfully was operated upon that we deemed it well worthy of being placed upon record.

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ABSTRACTS

FLOYD H. JERGENSEN AND J. P. SIMONDS.

The Blood Lipase in Patients with Peptic Ulcer. Its relation to hepatic and pancreatic disease. Jour. Lab. and Clin. Med. XIX. July, 1934 (1051-1058).

Originally it was thought by Cherry and Crandall that lipase appeared in the blood stream only in diseases of the liver and of the pancreas.

In a series of fifty cases of definitely proven peptic ulcer, a blood lipase titer equivalent to .3 c.c. of N/20 sodium hydroxide or greater, was found in thirty-eight instances, or 76 per cent. All four cases of gastric ulcer studied showed an increased lipase titer.

In a control series of twenty-five cases, only three gave positive results using the above criterion. From the statistics, it is concluded that 76 per cent of the ulcer-bearing patients had an associated dysfunction of the liver. The amount of the lipolytic enzyme was shown to be without relation to the age or sex of the patient, or to the duration of the symptoms.

H. J. Wolff, Rochester, Minnesota.

FRED K. HECK AND HAROLD M. MORTIMER.

Carcinoma of the Pancreas. Jour. Lab. and Clin. Med. XIX. July, 1934 (1058-1067).

In a series of 50 proven cases of primary pancreatic carcinoma occurring in the course of 7,932 autopsies, this lesion represented 5.3 per cent of all malignancies, and was one-fourth as common as is gastric carcinoma. There was a large preponderance in males (corrected statistical ratio: 41 males to 18 females).

In the pancreas, the location of lesions was in the head twenty-two times, in the body or tail twenty-three times, and throughout the entire organ four times. This percentage ratio (46 per cent in the body or tail) contrasts markedly with the statistics usually offered.

The three most constant *symptoms*, in order of statistical importance were pain and weight loss, then anorexia, and finally jaundice. Independently Kiefer and Speel previously reported cachexia and weight loss as the most outstanding signs, followed in order by jaundice and pain. Here again, the new report serves to illustrate the variability that may be expected.

The pain usually was epigastric and of differing intensity; it radiated around the costal margin in some cases; in others into the chest (pseudo-angina); in still others into the groin (ureteral involvement); and finally, in fifteen cases into the back. In most of the latter group, the lesion was in the body of the gland. Relief from back pain could be obtained by sitting erect or walking bent forward.

Jaundice was not so commonly seen as might be inferred from the writings of Bard and Pic; it was, in fact, absent in three of the twenty-two cases showing involvement of the pancreas' head. Strangely, in one instance, jaundice appeared, receded, and then reappeared six months later with renewed intensity.

The absence of diarrhoea was emphasized by the frequency of constipation; only one case in forty-six developed diarrhoea; fatty stools were not found in this instance.

On *physical examination*, a mass, firm, usually not nodular, but at times easily mistaken for liver, could be palpated in thirty cases. In three of these, the mass moved on respiration. Carcinomatosis of the peritoneum manifested itself in eight cases by ascites, and in three cases, by *cul-de-sac* involvement.

It was concluded that there is an early occurrence of widespread metastasis and that palliative treatment alone can be employed.

H. J. Wolff, Rochester, Minnesota.

Diverticula of the Jejunum

A Review of the Literature and the Report of Two New Instances*

By

JEROME S. LEVY, M.D.

and

A. De GROAT, M.D.

LITTLE ROCK, ARKANSAS

AMONG the diverticula which are observed in the various segments of the alimentary canal, those of the jejunum possess a special interest because of their rarity and obscure etiology. Most of the known examples of jejunal diverticula have been reviewed by Watson (1), Rothschild (2), Helvestine (3) and Evans (4). Since 1925, when Rothschild (2) collected thirty-three cases, the reports have been more frequent and at present, including our two cases, we have collected sixty-eight from the literature. Besides these proved cases there are three reported by Larimore and Graham (5), three of the five reported by Case (6), one by Heidecker (1), one by Swanberg (7) and one by Merkelbach (8), which were diagnosed by X-ray but not operated upon, and therefore, lack confirmation. If one adds these to the above number, a total of seventy-seven cases have been reported since Cooper (3) in 1844 reported the first case of jejunal diverticula. The cases composing this review do not include diverticula of the duodeno-jejunal junction. Fraser (9) quotes autopsy statistics of various authors who found diverticula of the small intestine "including jejunal" but no definite number of cases of jejunal diverticula was noted. Nor were the cases reported by Edwards (10) included, as he says: "In a series of ten specimens of hernial diverticula of the jejunum investigated, three are multiple, seven single. In two further radiological cases, the diverticula were multiple." He fails to state whether these are new cases or are included in those previously reported by others and so merely are restudied.

PATHOLOGY

From a study of the reported cases, it was found that the sacs usually occur along the mesentric border of the gut and in close relationship to the arteries and veins. It is this relationship which forms the basis of the generally accepted theory of etiology. As a rule they are multiple, as many as four hundred having been found in one case. Twenty of the seventy-seven cases culled from the literature were solitary; six of these being true instances, five having no notation in this respect. Practically all of the cases of multiple diverticula were "false", i. e., lacking in one or more of the coats of the intestine (only two of the forty-one cases of multiple diverticula were reported as being "true"). Six of the seventy-seven cases are reported arising from the anti-mesentric border; all but one were true diverticula. These probably are congenital in origin.

Microscopically, the muscle layers of the gut are usually missing, although occasionally one may find the longitudinal layer in the wall of the pouch. When present it shows evidence of atrophy. The absence or presence of both muscle layers distinguishes the true from the false diverticula. Figure 1 shows a typical microscopic picture. The mucosa, submucosa, longitudinal muscle layer and the serosa are present. There is a degeneration of the mucosal elements and the muscle layer shows marked thinning and atrophic changes. The circular layer of muscle is absent. Figure 2 was taken through the neck of the pouch in Case No. 2 and shows the thinning out and loss of the circular muscle fibers. Occasionally, the mucous membrane and submucosa show inflammatory changes. Microscopic study then reveals an infiltration of the mucosa by polymorphonuclear leucocytes, lymphocytes and plasma cells. Either

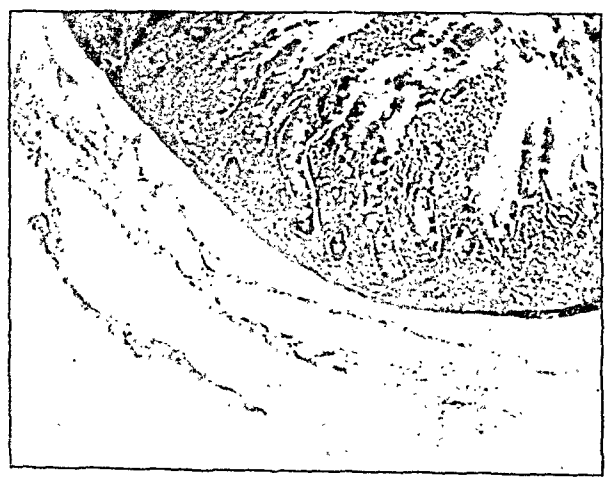


Fig. 1. Section through wall of the diverticulum in Case 2. The mucosa, submucosa, longitudinal muscle layer and serosa are present. The muscle coat is exceptionally thin. The circular coat of muscle is absent.

*From the Departments of Medicine and of Pathology, respectively, University of Arkansas School of Medicine, Little Rock, Arkansas.

Submitted September 27, 1934.

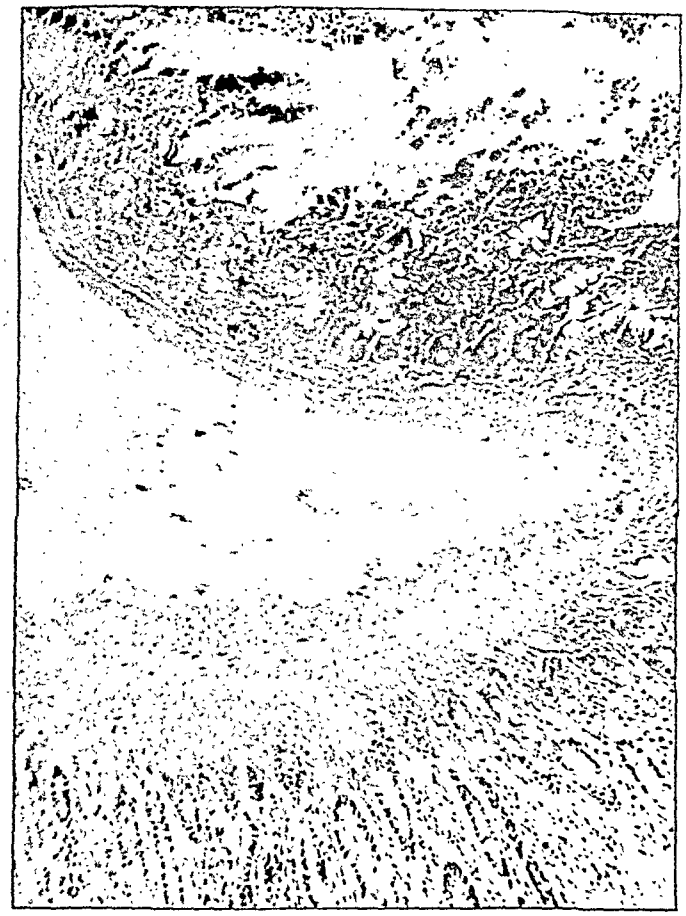


Fig. 2. Section through the neck of the diverticulum in Case 2. The portion of the wall of the jejunum shows the usual coats of the intestine. Note the disappearance of the circular fibers of muscle along the wall of the sac.

acute or chronic changes may be present.

ETIOLOGY

The cause of jejunal diverticula is obscure. Klebs (3) in 1867 pointed out the definite relationship between the mesenteric blood vessels and the diverticula, each of the latter arising at a point at which one of the *vasa recta* of the superior mesentric artery enters the bowel wall (Figure 3). This predisposes to a weakening of the wall and subsequent herniation. Substantiation, at least in part, is furnished by the usual lack of the muscle layers in the walls of the diverticula, which show, generally, on microscopic study, only mucosa, submucosa with its few fibers of muscle, and serosa. If either of the muscle layers are present it is the longitudinal muscle which shows definite thinning and atrophy. The commonly accepted theory is that these diverticula start out as small pouches, containing all the coats of the intestine, herniating through the weakened passage along the blood vessels. Subsequently, the muscle layers in the sac which already were the seat of some changes further atrophy and disappear. As the vessels alternate from one side of the gut to the other, so do the small pouches. As they enlarge, the sacs become confluent and thus one large pouch is formed; its mouth straddles the mid-line of the mesentric border of the intestine. The fact that the majority of these anomalies occur in elderly people adds further weight to this theory. Klebs thought that the traction of the mesentery was an added factor.

Hanseman (3), 1896, attributed importance to the increase in pressure within the gut lumen, while Grasser (3), 1899, believed that congestion in the mesenteric veins caused a separation of the muscle bundles and produced diverticula. Roth (3), 1872, advanced the theory that fatty degeneration of the *tunica muscularis* was the dominant factor. Sudsuki (3), 1900, attributed importance to the diminished resistance around the veins, with changes in the connective tissue. Edwards (10) recently has classified diverticula of the duodenum and jejunum as follows:

A—*Congenital Diverticula*
- 1—Meckel's diverticulum
- 2—Non-Mecklian diverticulum
 - (a) Giant diverticulum
 - (b) Diverticulum associated with ectopic pancreatic tissue
 - (c) Cyst-like diverticulum

We believe a fourth group should be added here:

 - (d) Simple, "true" diverticulum

B—*Acquired Diverticula*
- 1—Primary
- 2—Secondary
 - (a) Diverticulum due to disease of the bowel wall; e. g., ulcer producing a diverticulum of the duodenum
 - (b) Traction diverticulum
- 3—Pseudo-diverticulum.

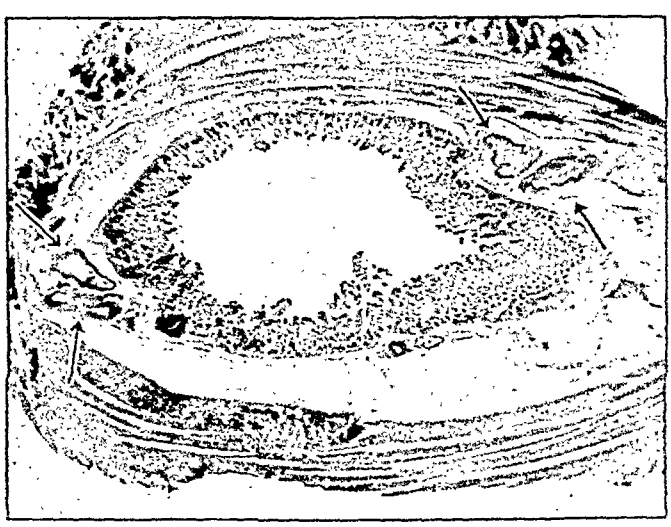


Fig. 3. Case 1. A transverse section through the neck of a small diverticulum as it passes through the muscular coat of the jejunum. On each side is a mesenteric vein and artery (shown by arrows).



Fig. 4. Case 2. Reproduction of six-hour X-ray film. The arrows point to the diverticula of the jejunum filled with barium.

SIGNS AND SYMPTOMS

The *symptomatology* varies from a complete absence of functional disturbance to those of obstruction or perforation. Many diverticula were found at autopsy; a review of the case histories failed to disclose any symptoms referable to the diverticula. On the other hand, a number of cases had been subjected to emergency operations for acute abdominal symptoms due usually to acute obstruction secondary to changes of various sorts in the jejunal diverticula. A few others caused epigastric discomfort, in some instances this amounted to actual pain, arising at varying intervals after meals; this discomfort may or may not have been relieved by soda, thus simulating peptic ulceration. Still other diverticula seemed responsible for symptoms of a less definite type, such as bloating and fullness, "gas rumbling" and an indefinite or vague uneasiness after meals. It is readily realized, then, that the clinical history offers no definite clue to the diagnosis.

Physical examination, likewise, may fail to arouse the suspicion of a diverticulum. Acute abdominal signs, when they demand immediate surgery, offer no problem for the pouch may be found at operation. In other cases, the routine physical examination may be entirely negative. However, there may be a point of localized tenderness just to the left and above the umbilicus. This clue may be the only one and, even then, may not be present unless there are inflammatory changes in the pouch.

X-RAY EVIDENCE

Since the first report of a positive X-ray diagnosis made by Case (6), nineteen cases have been reported so diagnosed. Of these, only ten have been operated upon, but the diagnosis was confirmed in each case. The second case reported in this paper will be the twentieth to be recognized by X-ray examination and the eleventh to be operated upon, thus confirming the prelaparotomy diagnosis.

The characteristic picture at X-ray examination is the appearance of a number of small pouches of persistently retained barium, usually with fluid levels, in the region of the jejunum. However, the solitary diverticulum may simulate the X-ray picture of a chronic perforating ulcer of the stomach or the duodenum. Two such have been reported: one by Briggs and Hurst (11) and one by Brohee (quoted by Briggs and Hurst). In each of these cases, however, the diverticulum was at the duodeno-jejunal junction. One of our instances simulated this picture at the first examination but subsequent study afforded the opportunity correctly to interpret the findings. The accompanying reproductions of the six-hour and seventy-two-hour X-ray films (Figures 4 and 5) show the diverticulum filled with barium. The legends are explanatory.

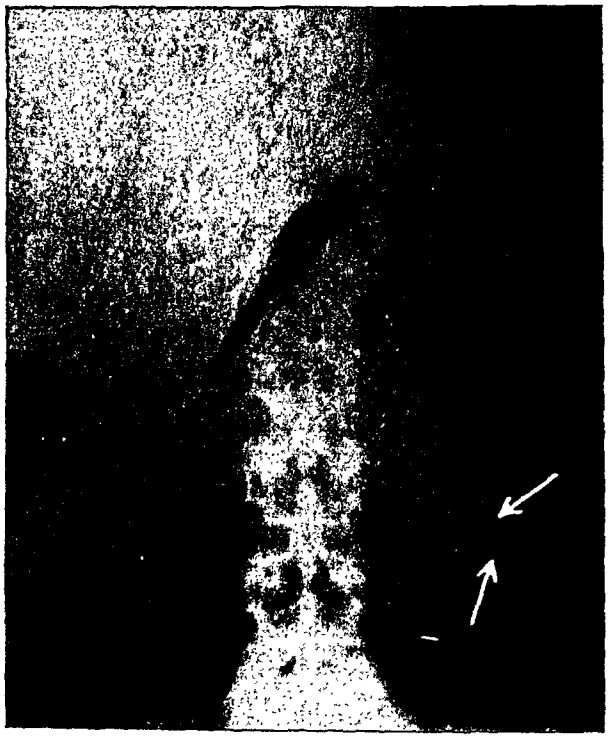


Fig. 5. Case 2. Reproduction of the seventy-two-hour film. The diverticulum remained filled with barium.

CASE REPORTS

Case No. 1—A vagabond, American Indian presenting symptoms of cardiac decompensation, died shortly after entering the Little Rock City Hospital. He appeared to be about 75 years old. The autopsy was performed by one of us (A.DeG.).

The autopsy findings, briefly, were extreme emaciation, generalized advanced arterio-sclerosis, cardiac hypertrophy and fibrosis, bilateral hydrothorax, ascites and chronic passive congestion of the liver and the spleen. There was a right hydro-nephrosis and hydro-ureter accompanied by marked atrophy of the renal parenchyma. The left kidney showed advanced atrophy from vascular changes and chronic pyelonephritis. A median lobe hypertrophy of the prostate gland was associated with hypertrophy of the bladder and chronic cystitis. In the base of the bladder were two small diverticula. The general changes in the gastro-intestinal tract consisted of congestion and moderate oedema.

On the mesenteric border of the first seventy-five centimeters of the jejunum were *twenty diverticula* which varied in size from three to forty-five millimeters (Fig. 6). The smaller lesions were discovered by dissecting the blood vessels entering the bowel. All projected to the left side of the mesentery. They were of the "false" type and communicated with the intestine by wide orifices (Fig. 3). Particular attention was paid to the small diverticula and sections of the entire specimen were made in four of them and these were examined microscopically. In none did it appear that the muscular coat of the bowel had entered into the formation of the sac. For example, in a diverticulum having a transverse diameter of slightly less than three millimeters, the circular layer of the intestinal musculature was seen to stop short at the neck while, on one side only, the longitudinal layer extended over the surface of the sac a distance of one and a half millimeters. The relation of the sac and the mesenteric vessels is shown in Fig. 3. The vessels at this level were not appreciably sclerotic. The muscle coat of the jejunum was remarkably thin, measuring two millimeters and less.

Case No. 2—This patient, Mrs. E. T., age 42, entered the hospital on the gastro-intestinal service of one of us (J.S.L.). She complained of a burning and "hurting in the stomach" which had been present off and on since a first attack ten years before; this initial upset was characterized by a fairly persistent siege of vomiting, which she alleged lasted nearly a year. There had been a daily occurrence of epigastric burning since, aggravated each spring. A gnawing sensation frequently was experienced from which the ingestion of soda gave but slight relief. She also had a cramping pain in the pit of the stomach which would begin immediately after eating and would last three hours unless relieved by soda. There was a definite intolerance to raw apples, onions, sweets and fried, greasy foods.

There was a family history of tuberculosis. The patient's father and mother had died with this disease; her husband had an advanced bilateral pulmonary involvement; two children had arrested tuberculosis and one other had an active pulmonary tuberculosis. The patient, herself, had been in a sanatorium for repeated pulmonary hemorrhages but careful study by us failed to reveal evidence to justify a positive diagnosis of tuberculosis. However, there was a bilateral bronchiectasis which we believed to be the cause of the hemorrhages, one being observed while the patient was in the hospital.

Examination disclosed a small area of abdominal tenderness localized to the left of the mid-line just above the level of the umbilicus. Except for persisitent traces of albumin in the urine the remainder of the examination was negative. However, the *X-ray* studies were illuminating. The patient was given a barium meal and routine observations made. At the time of the first examination a large pouch, along the greater curvature of the stomach and to the left of the mid-line, was noted. No other findings involving the stomach or the duodenum were recorded. At six hours, the barium had reached the colon but there was a definite retention of the barium in the pouch above mentioned. There was a noticeable tenderness to pressure over it and this tenderness coincided with the area of tenderness noted during the general physical examination. The appendix was filled, irregularly so, thinned, and there was tenderness associated and limited to the appendix shadow. This was noted again at the twenty-

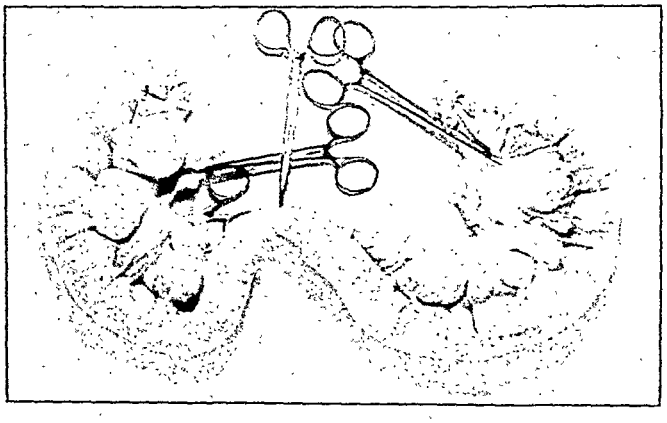
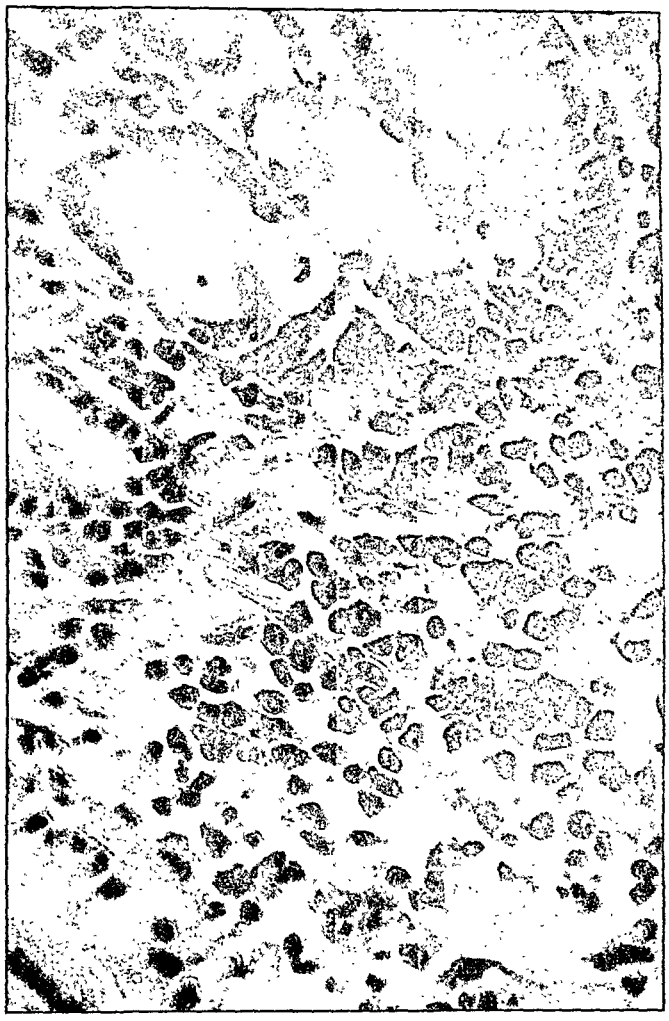


Fig. 6. Case 1. Portion of the jejunum with numerous diverticula along the mesenteric border. Gross autopsy specimen.

Fig. 7. Case 2. High power study of mucosa of diverticulum. There is an infiltration by plasma cells, lymphocytes and polymorphonuclear leucocytes.



Author	Year	No. of Cases	Multiple or Solitary	Type	Origin	Remarks
Cooper	1844	One	Multiple	False	Mesenteric	First recorded; found at autopsy.
Cornilliac	1869	One	Solitary	False	Mesenteric	Found at autopsy.
Neuse [illegible]	1870	One	Solitary	True	?	Found at autopsy.
Ochs	1881	One	Multiple	False	Mesenteric	Found at autopsy.
Mayo	1884	One	Multiple	True	"	Found at autopsy.
Fenwick	1885	One	Solitary	True	"	Found at autopsy.
Pozzi	1890	One	Multiple	False	"	Found at autopsy.
Brockwell & Jacobi	1890	One	Multiple	False	"	Found at autopsy.
Virchow	1890	One	Multiple	?	"	Found at autopsy.
Ewel	1894	One	Multiple	?	"	Found at autopsy.
Siegel	1895	One	Multiple	False	"	Found at autopsy.
Gaul	1895	One	Multiple	False	Anti-Mesenteric	Found at autopsy.
Hansemann	1896	Two	Multiple	False	Mesenteric	Found at autopsy.
			Solitary	"	"	
Grossberger	1897	One	Solitary	"	"	Found at autopsy.
Nichols	1899	One	Multiple	"	"	Found at autopsy.
Hedenyi	1900	One	Multiple	"	"	Found at autopsy.
Lecher	1901	One	Solitary	"	"	Found at autopsy.
Gardner & Sampson	1905	One	Multiple	"	"	Found at autopsy.
Taylor & Lakin	1910	One	Multiple	"	"	Found at autopsy.
Balfour	1913	One	Multiple	"	"	Found at autopsy.
Lenarjet & Murad	1914	One	Solitary	"	"	Found at autopsy.
Braithwaite	1918	One	Multiple	"	"	Found at autopsy.
Aberlund	1918	One	?	?	?	Quoted by Watson.
Case	1920	Five	Multiple	False	Mesenteric	Diagnosed by X-ray; two confirmed by operation, others not operated on.
McWilliams	1921	One	Multiple	False	"	Quoted by Helvestine.
Terry & Murfee	1921	One	Multiple	False	"	Quoted by Helvestine.
Miller	1921	One	Solitary	True	Anti-Mesenteric	Diagnosed by X-ray with operative confirmation.
McKechnie	1921	One	Multiple	False	"	Quoted by Helvestine.
Cook & Hunt	1921	Two	Multiple	"	Mesenteric	Diagnosed by X-ray, operative confirmation, autopsy.
			Solitary	"	"	
Hunter, J. S.	1922	One	Multiple	?	Mesenteric	Quoted by Evans—found in a 7-day-old child.
Braithwaite	1923	One	Multiple	?	?	Diagnosed by X-ray, confirmed by operation.
Helvestine	1923	Two	Multiple	False	Mesenteric	Both found at operation.
			Solitary	"	"	
Watson	1924	One	Solitary	"	"	Diagnosed acute obstruction (sigmoid), operation showed diverticulum of jejunum causing obstruction.
Bastrop	1924	One	Solitary	?	?	X-ray diagnosis, operative confirmation. Quoted by Fraser.
Sleppy	1924	One	Multiple	False	?	Found at autopsy. Quoted by Rothschild.
Swardberg	1925	One	Solitary	?	?	Diagnosed by X-ray; no confirmation.
Rothschild	1925	One	Solitary		Anti-Mesenteric	Diagnosed by X-ray, confirmed at operation.
Herbecker	1926	One	?	?	?	Diagnosed by -Xray. Quoted by Watson.
Larimore & Graham	1927	Three	?	?	?	X-ray examination showed diverticula of jejunum, no operative confirmation.
Brixton	1927	One	?	?	?	Quoted by Godard.
Moreau & Murdock	1927	One	?	?	?	Quoted by Godard.
Godard	1927	One	Multiple	False	Mesenteric	Found at operation for acute intestinal obstruction.
Berry	1927	One	Multiple	?	"	Found at autopsy.
Simons	1928	One	Multiple	?	"	Found at operation for "acute abdomen".
Fort	1928	One	Solitary	True	Anti-Mesenteric	Found at autopsy.
Lambret & Surmont	1928	One	Multiple	?	Mesenteric	Noted but not recognized by X-ray, found at operation.
Tenewall	1930	One	Multiple	True	"	Not recognized by X-ray, found at operation.
Somerford	1930	One	Solitary	?	"	Found at operation—considered congenital.
Gilbert	1931	One	Multiple	?	"	Found at operation
Bolme	1931	One	Multiple	False	"	Not recognized by X-ray, found at operation.
Biegler, Bloom & Wrable	1931	One	Solitary	True	"	Diagnosed by X-ray, confirmed at operation.
Orlean	1932	One	?	?	?	Quoted by Fraser.
Miller (2nd)	1932	One	Solitary	True	Anti-Mesenteric	Diagnosed by X-ray, confirmed by operation. Similar case to his reported in 1921.
Leriche	1932	One	Multiple	False	Mesenteric	Observed by X-ray, not interpreted correctly, found at operation.
Christ	1932	Two	Multiple	?	Mesenteric	Both found at operation.
Fraser	1933	One	Multiple	False	"	Found at operation. X-rayed after operation and found them then.
Butler	1933	Seven	Multiple	False	"	One diagnosed by X-ray; two by autopsy; other four were cases not reported before.
Flynn	1933	One	Multiple	?	"	Found at operation.
Merkelbach	1933	Two	Multiple	?	?	Incorrectly called carcinoma at X-ray examination. Found at operation. One solitary, seen on X-ray film—not corroborated.
			Solitary	?	?	
DeGroat (See Text)	1934	One	Multiple	False	Mesenteric	Found at autopsy.
Levy (See Text)	1934	One	Solitary	False	"	Diagnosed by X-ray, confirmed by operation.

Chart I. Compilation of Reported Cases of Jejunal Diverticula. The above chart includes the probable cases of diverticula (based on X-ray findings but without confirmation) as well as all proved cases. The Authors acknowledge their debt to Helvestine for material dated previous to 1918.

four hour examination, as also was the barium-filled pouch, likewise tender. The patient was given a second barium meal and the relations of the pouch studied. It was then recognized as a diverticulum of the first portion of the jejunum. The patient was given the gall-bladder test dye by mouth and films were taken at twelve, sixteen and twenty hours. No shadow was seen on either film, from which observation it was concluded that the gall bladder was non-functioning. A *diagnosis* of a diverticulum of the jejunum, pathologic appendix, pathologic gall bladder, and an irritable colon, spastic type, probably secondary to the above causes, was made.

When patient was *operated* upon by Dr. George V. Lewis, the gall bladder was found to be thickened, enlarged, and with adhesions between it and the duodenum. The appendix was thickened, injected, and grossly pathologic. The diverticulum was found along the mesenteric border of the jejunum four or five centimeters distal to the duodeno-jejunal junction. A purse string suture of silk was placed at the neck of the sac, the diverticulum amputated, the suture tied and the stump invaginated. A double row of Lembert sutures was introduced. The gall bladder and appendix were removed with the usual technique.

The *pathologist* (A.DeG.) *reported* chronic cholecystitis, chronic appendicitis, and a "false" diverticulum of the jejunum with inflammatory changes in its wall. The microscopic picture of the diverticulum has been described in the body of the paper (Figs. 1 and 2). For the past year and a half the patient has been relieved of most of her gastro-intestinal symptoms, except an obstinate constipation. She does very well on a high vitamin, low residue diet and mineral oil. Economic conditions prevent constant adherence to the prescribed diet. She has had several pulmonary hemorrhages.

CONCLUSIONS

(1) A review of the literature reveals sixty-six authentic cases of diverticula of the jejunum. There are nine other probable cases, i. e., diagnosed by X-ray but in whom operation has not been permitted and the diagnosis, therefore, not com-

pletely confirmed. The present authors report two additional cases, proved anatomically, one by autopsy, one by operation. These instances now bring the total to seventy-seven.

(2) One of the cases reported herein is the twentieth diagnosed by X-ray and the eleventh in whom operation later was performed with confirmation.

(3) Symptoms of diverticula of the jejunum may vary from a complete absence of digestive disturbances or abdominal anomaly to those of an acute abdominal lesion. The history of peptic ulceration may be simulated.

(4) The etiology of jejunal diverticula has been discussed and the gross and microscopic anatomy has been described.

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"Okrin" As An Adjuvant in the Treatment of Peptic Ulcer*

Observations Upon Twenty-two Patients

By

ARTHUR J. ATKINSON, M.D.
CHICAGO, ILLINOIS

AN ADJUVANT in the medical management of peptic ulcer was added with the introduction of gastric mucin by Fogelson (1). The beneficial action of gastric mucin in ulcer may be due to its viscosity and demulcent properties enabling it to protect the ulcer from chemical and mechanical irritation or to its anti-peptic activity. It is also probable that some individuals with chronic ulcer are deficient in the secretion of mucus, the hypersthenic stomach of Hurst (2). Gastric mucin may supply the mucus needed or it may influence the synthesis of mucus by the mucous membranes because it contains glycuronic acid which would appear to be necessary for the formation of mucin. Even though in ulcer treatment we may not admit the specificity of mucin, we believe that emollients have a place in our therapeutic armamentarium. Olive oil, cream, and other fats had been used for years before the use of mucin, for a protective action as well as a secretory depressant action. An excess of fat, however, causes nausea and delays the emptying of the stomach. Mucin has been thought by some to be unpleasant, and in some instances to contain "secretagogues", which increase the production of acid gastric juice. Being an animal product, it is subject, of course, to decomposition and putrefaction.

To overcome the objections to mucin we attempted to find a vegetable substance which would

*From the Departments of Physiology and Medicine, Northwestern University Medical School.
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have a rich yield of mucinaginous material and contain glycuronic acid. Among the plants studied by us the pod of the okra plant (*Abelmoschu esculentus*) seemed most suitable. The mucilaginous material was extracted from the pods, and converted into a fine powder which we called "okrin". The details of the method of extraction and the physical and chemical properties of okrin can be found in our preliminary report (3). Okrin is exceedingly viscous in aqueous solution and has an okra odor and taste. The okrin used was entirely free of secretagogues when tested on a dog with a pouch of the entire stomach.

MATERIAL STUDIED

For the past two years we have been using okrin in the treatment of peptic ulcer in twenty-two selected patients. Three other patients, after preliminary treatment, did not return to the Clinic and could not be reached. Patients in the gastro-intestinal clinic having the most difficulty on other managements were chosen for this probatory period. This method of selection of patients attempted to eliminate that large percentage of ulcer patients which has temporary remissions after any type of treatment.

All patients had history, signs, symptoms, laboratory evidence and roentgen manifestations of peptic ulcer. Ewald test meals, fractional and motor test meals and examination of stools for occult blood were performed.

This series includes one patient affected with a prepyloric ulcer. There were eight patients who previously had had gastro-enterostomy performed, with recurrent lesions at the stoma or in duodenal bulb or both. Thirteen patients had duodenal ulcers. Some had the complication of gastric retention and a definite continuous secretion as evidenced by retention and night distress. The chronicity of the ulcer diathesis is indicated by the 4.2 years average duration of periodic pain.

METHOD OF TREATMENT

Four to eight grams of okrin were taken in water, milk, canned milk, or milk and cream every hour while the patient was awake. Most patients were allowed three smooth, bland, low secretagogue-yielding meals daily, with adequate vitamins and minerals, but if there was marked retention or vomiting, feedings were begun gradually. All patients were treated while ambulatory.

RESULTS OF TREATMENT

In seventeen of the twenty-two patients remission occurred in from one to ten days. There was an absence of pain during the day, a cessation of vomiting and pyrosis, and diminution of night distress within the first two or three days. During the next two weeks there was a disappearance of the night distress, of epigastric tenderness and of blood from the feces. Re-examination gave roentgenographic evidence of decreased pylorospasm and decreased emptying time. It was not possible to give a definite opinion of anatomical changes in the lesions except in those prepyloric ulcers with niche formation which roentgen anomaly disappeared after treatment. Three patients with duodenal ulcer and two with jejunal ulcers failed to obtain relief. Some of the failures in this "intractable" group might have had complicated ulcers with accompanying perigastritis or periduodenitis and peritoneal adhesions causing pain. Surgical intervention may be necessary to relieve them. There is also the possibility of cicatrised ulcer being the cause of continuous discomfort along with gradually increasing stenosis due to cicatricial contraction and fibrous connective tissue thickening at the border of the ulcer. Ten patients after preliminary treatment did not take okrin for periods of from one to six months. Three of these had recrudescences which again were relieved by okrin.

COMMENT

In April, 1933, a preliminary report (3) was made of the use of okrin for peptic ulcer. At that time the supply of okrin was extremely limited, so that its use was confined to three patients. The results were sufficiently favorable to warrant additional investigation. Meyer, Seidmon, and Necheles (4) confirmed our original report.

Further study indicates that okrin relieves pain in patients with peptic ulcer and apparently produces a remission in a large percentage of ulcer-bearing individuals. We cannot prove that the ulcer has been healed, but the rapid relief of pain may indicate a subsidence of accompanying gastritis and duodenitis.

A direct comparison of the benefit of okrin with gastric mucin cannot be made in a disease whose natural history is so variable. It was our impression that patients taking okrin did not gain in weight so rapidly as those taking mucin.

Okrin is pleasant to take and produces no untoward symptoms. It does not deteriorate or putrefy. Okrin, apparently, has a palliative, demulcent, protective action. It should be considered as an adjuvant to other previously proved methods of treating the peptic ulcer patients' general condition.

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SECTION II—*Experimental Physiology*

The "Chemical" Phase of Gastric Secretion and Its Regulation*

By

B. P. BABKIN, M.D., D.Sc., F.R.S.C.†
MONTREAL, CANADA

WHENEVER I speak before a medical audience on the physiology of the gastro-intestinal tract, I feel somewhat guilty lest I be communicating things which have at the present time very little or no practical value. Gastro-enterology today is chiefly an empirical science—the theory and the practice in this field of knowledge stand at present so far apart. But the history of physiology and of medicine makes me strongly believe that the time will come when practical medicine will need and will use everything that physiology knows. In this connection it is enough to remember the case of the string galvanometer, now an indispensable clinical apparatus, which was originally constructed by a physiologist, and the idea of which grew out of some purely physiological investigations, or the case of insulin, the use of which was made possible in modern medicine because some sixty-five years ago Langerhans (1869) discovered the islet tissue in the pancreatic gland and Laguesse (1893) propounded the theory of its anti-diabetic function. I am convinced that the more often the clinician and the physiologist come in contact with each other and talk over the things in which they are both interested, but on which they frequently look from different angles, the better it will be for medicine and for physiology.

Therefore, I hope you will pardon me if, in discussing the regulation of the secretory activity of the stomach during its second or chemical phase, I shall take you tonight, so to speak, to the laboratory of physiological thought, and shall tell you about our findings and failures, our hopes and disappointments.

It is a matter of common knowledge that the gastric secretion is regulated in at least two different ways: (1) through the nervous system, in the form of reflex action, and (2) through the body fluids, in a humoral way. The first of these mechanisms produces the *nervous phase of gastric secretion* (which comprises unconditioned and conditioned gastric reflexes). The second is responsible for the *second or chemical phase of gastric secretion.*

The nervous system influences the gastric secretion through the parasympathetic and sympathetic nervous systems. The vagus nerve contains presumably two kinds of secretory fibres: (a) those which produce regular gastric juice, and (b) those which activate the flow of mucus (Vineberg, 1931). There is solid ground for believing that different constituents of the gastric juice, namely, acid, pepsin, dissolved mucin and so on, are secreted by different cytological elements of the gastric mucosa (Babkin, 1931). We know of at least four groups of cells in the gastric mucosa—peptic cells, parietal cells, mucoid cells and mucous cells of the surface epithelium. The three first-named groups of cells are activated by the first type of vagus fibres; the last group—surface epithelium cells—by the second type of vagus fibres. The sympathetic nervous system is responsible chiefly for the secretion of mucus (Baxter, 1934, a and b).

I shall restrict myself to these few remarks concerning the nervous phase of gastric secretion. Our chief interest will be centered tonight in the second or chemical phase of gastric secretion. This phase is no less interesting from the clinical point of view than the nervous phase of gastric secretion. That such a phase exists is an established fact, but the mechanism by which it is produced is not at all clear.

The fundamental fact on which the idea of a "chemical phase" is based is illustrated by experiments in which the nervous phase is eliminated in an animal or a human subject, the food being introduced directly into the stomach through a fistula or a gastric tube. After a certain latent period the gastric glands begin to secrete. The "chemical phase" may be subdivided into two phases, the "pyloric" and the "intestinal". The existence of the pyloric phase is proved by the following experiments (see Babkin, 1928):

(1) In a dog with a gastric fistula, Pavlov pouch and duodenal fistula, and the fundus dis-

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†From the Department of Physiology, McGill University, Montreal.

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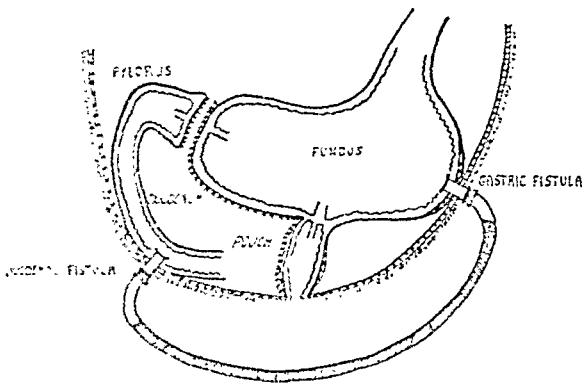


Fig. 1. Diagram of the gastro-intestinal tract of a dog with a gastric (metal) fistula, Pavlov pouch, duodenal (metal) fistula and the stomach divided into two parts at the boundary between the fundus and the pyloric part.

connected from the pyloric part, the introduction of food substances into the fundus through the fistula, with the exception of alcohol and histamine, did not provoke any secretion from the pouch or from the stomach (Figure 1).

(2) In a dog with a gastric fistula and Pavlov pouch and the whole stomach separated from the duodenum, the same food substances, on being introduced through the fistula into the stomach, produced a secretion from both pouch and stomach (Figure 2).

(3) The introduction of different chemical substances, such as meat extract, acetic acid, soap, etc., into an isolated and non-denervated, or even into a denervated pyloric pouch, caused a flow of juice from the fundus (Figure 3).

The last-mentioned finding has been challenged recently by Priestley and Mann (1932). The negative results obtained by them, however, might be partly explained by the methods which they employed. In one series of experiments the effect of a test-meal or injection of 1 mg. histamine was investigated before and after extirpation of the pyloric part of the stomach in the dog. No marked change in the acidity of the gastric juice was noted. This is what one would as a matter of fact expect, because with the test meal the predominant factor was the nervous phase, and the participation of the pyloric part in the stimulation of the peptic glands set up by the subcutaneous injection of histamine is rather doubtful. The volume of the secretion was not determined in these experiments. In a second series of experiments Priestley and Mann introduced different substances into an isolated pyloric pouch but failed to obtain a secretion from the stomach pouch. It is true that one of the substances which they used, namely, beef extract, is a recognized stimulant of the gastric secretion, but two others (tenth normal HCl and gastric juice) are known to inhibit the gastric secretion on coming into contact with the pyloric mucosa (Sokolov, 1904). It must further be added that Savitch (1922a) noted a state of gastric hypersecretion after isolation of the pyloric part of the stomach, during which the secretagogue effect of the gastric stimulants introduced into the latter was not very marked. Again, to obtain a definite secretagogue effect from these stimulants it was necessary to introduce them regularly day after day into the isolated pyloric part, as was done in the case of one of Savitch's dogs with a denervated pyloric pouch.

Thus the positive results of the experiments of Savitch and Zeliony (1913), of Savitch (1922a) and of Cinnimata (1926), demonstrating the secretagogue action of certain chemical substances when they come into contact with the pyloric mucosa still remain quite convincing in spite of the negative results obtained by Priestley and Mann. Ivy (1930, p. 289) at the present time seems to be inclined also to admit that stimulation of the pyloric mucosa may influence positively the secretion from the peptic glands.

There are also indications that mechanical stimulation of the pyloric part of the stomach, and even of a "denervated" pyloric pouch, stimulates the fundic glands. Thus Zeliony and Savitch (1914) and Savitch (1922b) showed that mechanical stimulation of the isolated pyloric pouch increases the production of pepsin by the fundic glands. Lim and Hou (1929) and Lim, Hou, Chang and Feng (1930) demonstrated that an abundant secretion of gastric juice could be provoked by the action of objects, such as bones, on the pyloric mucosa.

The existence of the intestinal chemical phase of gastric secretion has been proved by the following experiments on dogs:

(1) Secretion, after feeding, in a whole stomach isolated according to Frémont's method (Frouin, 1899; Ivy, Lim and McCarthy, 1925).

(2) Secretion, after duodenal feeding, in the whole stomach obstructed at the pylorus (Scott and Ivy, 1931; Webster, 1932).

As an example of the second type of experiment I may quote the following, which was performed in our laboratory (Webster and Armour, 1932), and is illustrated in Figure 4. A dog with oesophagotomy, gastric and duodenal fistulae and obstruction of the pylorus was being given a diet of glucose, casein, cream, NaCl and vitamins (cod liver oil, tomato and orange juice). The curve of the gastric secretion shows two rises, which are undoubtedly due to the introduction of the nutritive mixture into the intestine. The morning secretion, when glucose and saline were given, was scanty. This was due not only to the slow rate of introduction of the food but also probably to slow formation of gastric stimulants in the intestine, because the same result, i. e., a latent period of three to four hours, was noted when the feeding was commenced with casein solution. Between 11:45 a. m. and 12 noon, 100 c.c. of cream and 10 c.c. of cod liver oil were given. This produced a marked inhibition of the secretion.

From 2 p. m. to 4 p. m. casein solution was given. The first rise was presumably due to the effect of glucose and soap, the second to the products of casein digestion.

Certain substances, such as fat, concentrated solutions of glucose, etc., inhibit the gastric secretion on being introduced into the duodenum.

From these experiments, and many others which I need not quote here, it is evident that certain substances, by virtue of their chemical properties provoke gastric secretion on coming into contact with the mucosa of the pylorus and small intestine. The mechanism by which these substances activate the gastric glands is not at all clear. We know, it is true, that the long reflex paths are not involved, nor short reflex paths, if these exist. This is evident from the fact that denervation of the whole stomach or of a pouch does not hinder the stimulatory effect of these substances. Moreover these chemical stimulants provoke secretion in a gastric pouch transplanted to another part of the body (Ivy and Farrell, 1925). On the other hand, the effect of local application of these stimulants to the fundic mucosa is, with the exception of alcohol and histamine, practically *nil*. And yet the glands producing the gastric juice are embedded in this mucosa. If short reflex paths do exist, their receptors in the mucosa ought to be stimulated locally by the chemical stimulants. However, this is not the case. Chemical stimulants also produce a secretion from the fundus, when introduced into the completely denervated pylorus (Savitch, 1922a). Therefore, they can act from the pyloric part of the stomach and from the small intestine on the fundic glands through the blood only.

The mechanism by which the peptic glands are activated during the second or chemical phase is more or less clear until we reach this point. From here on the problem becomes a very complicated one. There is no intention on my part to discuss the many theories that have been put forward in explanation of this phase of the gastric secretion. But consideration of a few definite facts relating to this problem may be interesting and useful. There are several ways in which chemical stimulants may act humorally on the gastric glands:

(1) By the formation of a specific hormone (sometimes called "gastrin"). This was the first theory suggested by Edkins (1906); it has been supported more recently by Savitch (1922a).

(2) By the absorption from the pyloric part of the stomach and from the small intestine of chemical stimulants present in the food or formed from it during digestion. These substances, which are carried in the blood to the gastric glands, are supposed to activate the secretory cells directly. The chief exponent of this opinion is Rasenkov (1925).

(3) The chemical substances or "gastric hormones" mentioned in point (2) after absorption may stimulate the gastric secretion, not by direct action on the glandular cells but (a) through the local gastric plexuses or (b) through the centers in the brain.

Let us discuss the possible *mode of action of chemical stimulants on the gastric glands.*

Attempts have been made by many workers to extract a hormone ("gastrin") from the pyloric mucosa. The results, however, cannot be considered quite satisfactory, because when a substance was extracted from the pyloric mucosa which was capable of stimulating the fundic glands it was always found to be contaminated with other substances. In other words, it was not specific. One remarkable point brought out in these investigations was that gastrin possesses many features in common with histamine. The earlier investigators, therefore, concluded that histamine and gastrin (Rothlin and Gundlach, 1921) and histamine and secretin (Barger and Dale, 1911) are identical. We now know very well that the latter is not the case. A secretin preparation can be obtained which does not produce vasodilatation, does not stimulate gastric secretion, does not cause the formation of the intestinal juice and which, probably, is not identical with cholecystokinin.

The same cannot be stated so positively of gastrin and histamine. There are many indications that histamine participates in the stimulation of the fundic glands. Thus recently Sacks, Ivy, Burgess and Vandolah (1932), using as a solvent 1 per cent H_2SO_4 and 80 per cent alcohol, obtained from hog's pyloric mucosa an extract which lowered the blood pressure and produced gastric secretion. The active substance was identified chemically as histamine sulphate or picrate. Histaminase, when added to this extract, destroyed its secretagogue property. These investigators concluded that their experiments offer strong evidence in favor of the view that in acid extracts of the pyloric mucosa histamine is the sole secretory excitant which is active when the extract is introduced subcutaneously. However, they add cautiously that "it has not been proved that histamine is the gastric hormone; neither

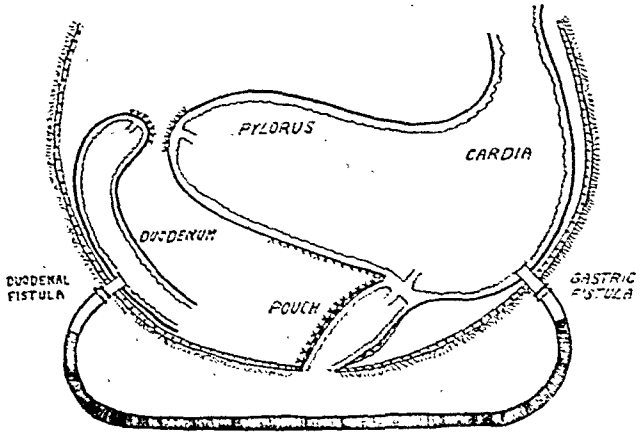


Fig. 2. Diagram of the gastro-intestinal tract of a dog with a gastric fistula, Pavlov pouch, duodenal fistula and the stomach separated from the duodenum at the pyloric sphincter.

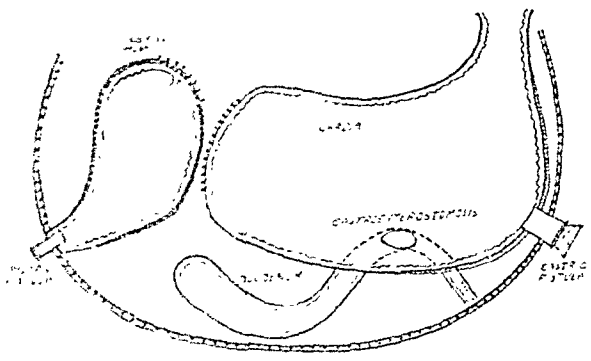


Fig. 3. Diagram of the gastro-intestinal tract of a dog with a gastric fistula, gastro-enterostomosis and an isolated pyloric pouch.

has it been proved that there *is* a gastric hormone".

Quite naturally the question arises: could not histamine be the hormone of the chemical phase? Tempting as it is on account of its simplicity, this theory cannot be accepted at the present time. That histamine does participate in some way in the mechanism of the chemical phase cannot be denied, but it would be incorrect to say that histamine is the *sole* hormone in this phase. The relations seem to be much more complicated. Thus:

(1) Histamine is very readily extracted by acids, yet the mineral acids, on coming into contact with the pyloric mucosa, do not stimulate gastric secretion and, in such concentrations as 0.3 to 0.5 per cent HCl, even inhibit it. Therefore, acid extracts of the pylorus undoubtedly contain histamine, but this does not mean that acid on coming into contact with the pyloric mucosa will liberate histamine.

(2) The chemical properties of the gastric juice secreted on histamine are somewhat different from those of the juice secreted during the second phase, although they have many common features. Thus, "histamine" juice is especially poor in organic constituents and nitrogen as well as in pepsin. Repeated subcutaneous injections of 0.75 to 1.0 mg. of histamine in a dog produce a gastric secretion with rapidly diminishing digestive power and nitrogen concentration (Babkin, 1930; Vineberg and Babkin, 1931; Gilman and Cowgill, 1931). Although the secretion in response to chemical stimuli may be of the same magnitude as the secretion produced by histamine, the concentration of organic substances and the peptic power of the former will be somewhat higher. The only exception is in the case of alcohol, which elicits a copious flow of gastric juice very poor in organic constituents.

(3) As was demonstrated above, in dogs with oesophagotomy, a gastric and a duodenal fistula, and obstruction of the pylorus, the gastric secretion continues for a very long time after the introduction of food mixture into the intestine. Could this secretion be due to the formation of histamine in the intestinal mucosa, or its liberation therefrom, under the influence of food masses? The small intestine, as was demonstrated by Best and McHenry (1930), contains a comparatively large amount of histamine, but at the same time its mucous membrane possesses an extremely strong histaminase. Could histamine, if it is formed in the intestine, be absorbed as such in these circumstances? This is not yet definitely proved. There is very meager evidence of the increased content of histamine in the blood after a meal. The experiments of Koskowski and Kubikowski (1929) and Koskowski (1933) could not be considered as affording proof of that. These investigators tested the effect of defibrinated blood on the uterus of a virgin guinea pig. The "fasting" blood hardly affected its contractions, whereas the "fed" blood (i. e., after a meal) produced a strong contraction. Among the substances which might be present in the blood, they found that histamine, choline and alpha-alanin are able to produce such an effect. The statement that the motor reaction observed in the uterus is due to histamine would, in these circumstances, be very inconclusive.

How complicated is the problem of the changing composition of the blood after ingestion of a meal is shown by the experiments of Rasenkov and his students (1927). They found that blood taken from a dog *before* it was fed did not produce any effect on the blood vessels of the isolated ear of a rabbit, or the frog's web, whereas the blood of the same animal *after* a meal acquired definite vasoconstrictor properties. This effect was not due to a greater output of adrenaline after the ingestion of food, since the same reaction was noted with the "fed" blood of adrenalectomized animals. Moreover, the coronary blood vessels of the isolated heart of a cat or rabbit were not influenced by the "fasting" blood, but were caused to contract by the "fed" blood, which does not indicate the presence of an excess of adrenaline in the "fed" blood. (The reaction of the coronary vessels to the "fed" blood is interesting from a clinical point of view, since an attack of angina pectoris often occurs after a meal.) Rasenkov's experiments were performed both on animals and on man, and gave analogous results. In patients with gastric hyposecretion or achylia gastrica, the blood did not acquire vasoconstrictor properties after a meal. Rasenkov ascribes the vasoconstrictor action of the "fed" blood to changes in its chemical composition.

Many of these data do not favor the theory that the second chemical phase is due to the liberation of histamine from the pyloric and intestinal mucosa and accumulation of this substance in the blood. And how may that histamine be liberated which is deposited in the fundic mucosa? Gavin, McHenry and Wilson (1933) showed that 80 per cent of the histamine content of the stomach is present in the fundic mucosa, and only 12 per cent in the pyloric mucosa. But the fundic mu-

cosa absorbs practically nothing. If its histamine is mobilized during secretion, some internal factor acting through the blood is responsible for this.

(4) Some very instructive experiments have been performed with atropine, although the results do not give a direct answer to the question of the *rôle* of histamine in the intestinal phase. Ivy, Lim and McCarthy (1925) demonstrated that in dogs, with the entire stomach formed into a pouch and the duodenum joined to the oesophagus, atropine inhibits the gastric secretion produced by different means. They did not study the secretion, however, after the effect of the atropine had passed. In similar experiments Webster and Armour (1932) used dogs with oesophagotomy, a gastric and a duodenal fistula, and the stomach obstructed at the pylorus. They collected the gastric secretion for a period of 24 hours. The animals, which were fed through the duodenal fistula, had, of course, only an intestinal phase of gastric secretion. Two milligrams of atropine sulphate stopped this secretion for three hours. However, when the effect of atropine had passed off, the renewed secretion compensated in volume for the temporary inhibition. Thus, for example, the day before the injection of atropine the total secretion for 24 hours in one of the dogs was 600 c.c.; on the day of atropine injection it was 630 c.c.; and the following day it amounted to 650 c.c. One of the explanations of this phenomenon may be that atropine prevented the formation in, or absorption from, the intestine of hormones or secretagogues (polypeptides, amino-acids, etc., *cf.* Ivy, 1930). The inhibition by atropine of pancreatic and intestinal secretions as well as of the motility of the intestine and the gall bladder, must also be taken into consideration. Thus, atropine indirectly may inhibit the formation of amino-acids, the splitting up of neutral fat and the formation of monosaccharides. As to the question whether histamine is liberated by the intestinal wall or absorbed from the chyme during intestinal digestion under normal conditions or after a small dose of atropine, we must frankly say that we do not know. But it is extremely doubtful that the inhibitory effect of atropine is due to the fact that it prevents the hormones already circulating in the blood from acting on the gastric glands, because during three or more hours they are either destroyed or eliminated. This statement cannot at any rate be applied to histamine if it is the "hormone" of the intestinal phase. It is a well-known fact that atropine does not interfere with the secretory effect of histamine on the gastric glands.

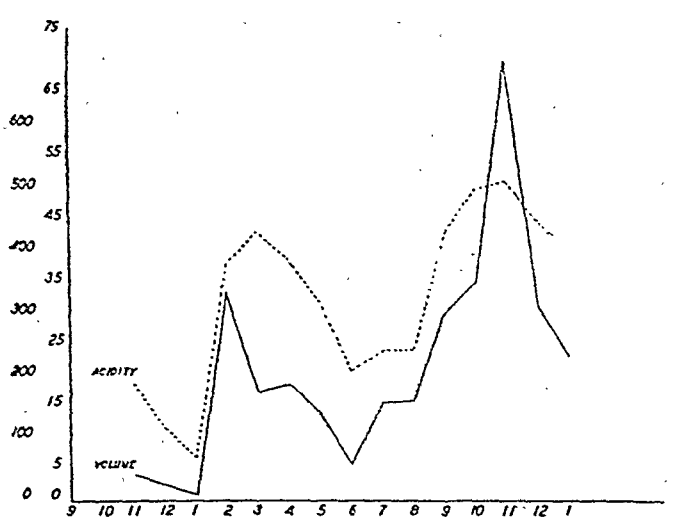


Fig. 4. The course of the gastric secretion and its total acidity (in mg. per cent) in a dog with oesophagotomy, gastric and duodenal (metal) fistulae and the stomach obstructed at the pylorus. The animal was fed through the duodenal fistula. (According to Webster and Armour).

We have obtained other data showing that the chemical phase cannot be attributed only to the effect of histamine on the secretory cells. Some preliminary results from our laboratory will be communicated here.

Extracts of beef meat and of different fish meats, deprived of fat, were introduced directly into the stomach of a dog, and their effects on gastric secretion were studied (J. Campbell, unpublished results). The secretagogue effect of these extracts was compared with that of the same amount of distilled water, tap water or physiological saline. In the control experiments, the greatest secretion occurred with distilled water, less with tap water and a negligible amount with saline. In order that the conditions in all the experiments might be the same the meat and fish extracts were diluted to the same osmotic pressure as the saline, and given in amounts of 200 c.c. It may be seen from Table I that the aqueous extract of meat gave approximately the same amount of secretion as did the extracts of fish, but the secretion from the meat extract lasted somewhat longer and was more acid, although it possessed a much smaller digestive power, than the secretion from the extract of fish. This fact is quite striking.

TABLE I

Secretagogue Action of Fish and Meat Extracts
(According to J. Campbell)
Dog with a Lesser Curvature Pouch and Gastric Fistula

Introduced 200 c.c. of extract of:	Duration of Secretion min.	Volume c.c.	Free HCl M.Eq./1 L.	Total HCl M.Eq./1 L.	Pepsin Mett's units
Cod	75	6.59	100	116	135
Haddock	75	6.28	98	113	117
Salmon	67	5.42	103	118	125
Meat	80	5.67	111	125	55

Since, on precipitation of the extracts, usually it was found that they contained about 1 per cent of protein nitrogen, our attention was directed towards the non-protein nitrogen fraction. The

silver-baryta method of Kossel and Kutscher was used for the isolation of the nitrogenous bases. As has been previously demonstrated (Krimberg and Komarov, 1926, 1928), the nitrogenous bases are those substances which are mainly responsible for the physiological activity (i. e., secretory power) of meat extract. The experiments of Dr. Komarov (1933, a and b) and of Mr. J. Campbell in our laboratory showed that extracts of the muscle of haddock and cod contain absolutely more nitrogenous bases than do extracts of meat, and relatively more, as a percentage of the total non-protein nitrogen. But the most striking fact was that, in the muscle of warm-blooded animals, the distribution of nitrogen between the histidine-arginine fraction and the lysine fraction was found to be in reverse proportion to its distribution in fish muscle. In the muscle of ox and horse the histidine-arginine fraction was larger and the lysine fraction relatively smaller, whereas in fish muscle the histidine-arginine fraction was considerably less than the lysine fraction (Table II).

TABLE II

Distribution of Non-Protein Nitrogen in Various Types of Muscle Expressed in Percentages of Total Non-Protein Nitrogen

(According to S. A. Komarov and J. Campbell)

Nitrogen in the form of:	Ox N.P.N. %	Horse N.P.N. %	Haddock N.P.N. %	Cod N.P.N. %
Nitrogenous bases	53.6		63.0	61.4
Histidine-arginine fraction	22.3	33.3	13.5	7.8
Lysine fraction	16.3	11.7	38.15	37.67

When these fractions were tested separately on gastric secretion, the histidine-arginine fraction produced a flow of juice which was abundant in volume but poor in enzymes, whereas the lysine fraction caused a scanty secretion of juice rich in enzymes. This may be seen in Table III. The

TABLE III

Secretagogue Action of Fractions of Cod Muscle

(According to J. Campbell)

Fractions of Cod Muscle	Total Nitrogen %	Volume c.c	Free HCl M.Eq. 1 L	Total HCl M.Eq./1 L.	Pepsin Mett'sunits
Whole extract	100	6.50	100	116	135
Nitrogenous bases	69	6.55	105	120	85
Histidine-arginine fraction	8	3.25	90	107	52
Lysine fraction	38	1.53			210

concentration of pepsin is seen to be four times greater in the gastric juice provoked by the lysine fraction than in the juice elicited by the histidine-arginine fraction, indicating the "choline-like" effect of the lysine fraction in contrast to the "histamine-like" effect of the histamine fraction. Therefore, the properties of the gastric juice were influenced by the chemical composition of the solutions introduced into the stomach.

Analogous results were obtained by Smith and Cowgill (1933), who demonstrated in dogs with a Pavlov pouch that some preparations of the extractive substances of meat produced a greater output of pepsin than did others, although the volume of secretion was the same.

The intimate mechanism involved in the action of different chemical substances on the gastric glands during the second phase has never been elucidated. But these experiments suggest that it may be of a double nature: chemical stimulants, or a hormone, if such exists, may act on the secretory cells (1) directly or (2) through the intermediary of the nervous system. The first supposition seems to be borne out by the experiments which the late Dr. Klein (1932, 1933) performed on a completely isolated and transplanted subcutaneous gastric pouch without myenteric plexus, which secreted in response to a meal and to histamine. It is not impossible that histamine is liberated from the gastric mucosa by some means (perhaps by a hormone) and stimulates the secretory cells. But the data on which the present communication is based show that histamine cannot be looked on as the *only* chemical substance which may stimulate the gastric secretion. There are other factors which must not be ignored: chemical stimulants, after they have been absorbed, may act on the peripheral nervous apparatus (gastric plexuses) of the stomach or even on the centers of the vagus and of the sympathetic. Might not certain substances, *e. g.*, those which are present in meat extract, after they have been absorbed, stimulate the neurones of the myenteric, and perhaps also those of the submucous plexus? This would lead to a greater discharge of enzymes, because we know very well that the activity of the peptic cells is under the control of the parasympathetic nervous system. In this respect it is very interesting to note the recent work of Kim and Ivy (1933), in which they studied the effect of atropine on the secretagogue action of vasodepressor-containing and vasodepressor-free extracts of liver and meat. Atropine prevented the secretagogue effect on the gastric glands of the vasodepressor-free extract when administered intravenously or introduced into the gastro-intestinal tract. On the other hand, the vasodepressor-containing extract, on being introduced intravenously, did not lose its power to stimulate gastric secretion after the atropinisation of the animal. The explanation of this phenomenon perhaps may be that non-purified extracts probably contained a certain amount of histamine or histamine-like substances.

There are some other facts which indicate that the presence or lack of certain chemical substances in the blood affects the gastric secretion through the central connections of the vagi. La Barre and Cespédès (1931), using the method of cross-circulation (in which the head of one dog—the "recipient"—connected with its body only by the vagi, was transfused with the blood of an-

other dog—the "donor"), showed that hypoglycaemia produced in the donor by insulin caused a gastric secretion in the recipient, whereas injection of glucose stopped the gastric secretion. Okada and his co-workers (1933) report that the gastric secretion provoked by insulin could be arrested by the injection of glucose, or of atropine, or by section of the vagi above the diaphragm. According to them, also the amino-acids (glycocoll, alanin, glutamic acid, histidine) and dipeptides such as glycylglycine, injected intravenously or given in large amount intra-intestinally, produce a gastric secretion. This secretion is inhibited by the injection of glucose or atropine. If in an animal the vagi have been previously cut above the diaphragm, these substances do not stimulate the gastric secretion.

Therefore, we may suppose that the chemical substances responsible for the pyloric and intestinal phases of gastric secretion act either independently or through the intermediary of a special hormone (the existence of which is still to be proved), *i. e.*, they act:

(a) directly on the secretory cells;

(b) through the intramural gastric plexuses; or

(c) through the centers in the brain, *via* the vagus nerves.

In other words, the "chemical" phase cannot be considered as exclusively humoral, since the nervous system also participates in it.

The discussion presented in this lecture does not strive to establish a new theory of the mode of stimulation of the gastric glands during the chemical phase of digestion. It has the more modest aim of communicating and recalling a few facts which will throw some light on this complicated problem. But I hope that it may serve as a useful "working hypothesis" which will facilitate further research in the field of the normal and pathological secretion of the gastric juice.

I come to the close of my lecture. The discussion presented to you may seem highly theoretical. But I am firmly convinced that the time will come when a gastro-enterologist may wish to regulate quantitatively the activity of the alimentary canal, and particularly of the stomach. He would then be eager to understand the mechanism regulating this activity, because only a full knowledge of all the conditions under which any machine works, especially one as complicated as the human body, can give command over its functioning.

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Accessible Closed Loops of the Small Intestine and the Colon*

By

G. E. BURGET, Ph.D.
PORTLAND, OREGON

SINCE its introduction by Whipple[1] and his associates, the closed intestinal loop has been used by many investigators to study the phenomena of obstruction. In an attempt to show a direct relationship between distension of a hollow viscus and clinical symptoms, we employed the closed intestinal loop but made it accessible by attaching its anti-mesenteric border to the body wall near the mid-line.[2] The loop, thus attached, remains available for puncture by a hypodermic needle. By thus entering the loop through the body wall at will the pressure or tension within the loop may be measured and the accumulated fluid drawn off.

By this surgical procedure we were able to carry on a thorough study of the relation of intestinal distension to clinical symptoms. Our observations, briefly, will be set forth below. Of even greater interest to the physiologist was the finding that, with care, these closed loops, sometimes termed "chronic loops," become normal segments of intestine which may be used to study absorption.

TECHNIQUE

A description of the technique used in making closed loops which are accessible is given here in briefest outline since the details may be obtained from earlier publications.[2,3]

Medium size dogs are used and aseptic surgical technique followed throughout. The peritoneal cavity is entered through a right rectus incision (left rectus if colon loop is desired[4]), two centimeters from the mid-line with the umbilicus marking the mid-point of the incision. The duodenum is picked up for orientation and a segment of the jejunum or ileum chosen for isolating. It should be 8 to 10 cm. long and have a good mesenteric blood supply which is not embarrassed when the segment is brought to the body wall. If a colon loop is desired this can be as readily made, provided the mesentery is of sufficient length. Its location is limited to the transverse portion or better described as the portion supplied by the right colic artery. The continuity of the intestinal tract is re-established by an aseptic end to end anastomosis and the loop attached to the anterior abdominal wall between the incision and the mid-line in the manner illustrated in Figures 1 and 2. The incision is closed leaving the loop accessible by thrusting a needle through the body wall over its attachment. This is done in the unanesthetized animal without evidence of pain since this area has been rendered insensitive by the original incision.

Dogs with closed loops thus attached do not show symptoms of obstruction unless the loop becomes distended with fluid. In this condition there is loss of appetite followed by vomiting unless the loop distension is relieved. Non-drainage of the distended loop results in diminished blood supply, necrosis, rupture and death.[2,5] Aspiration of the loop fluid when symptoms first appear almost immediately brings about the return of the animal to a normal state. Obviously the early symptoms are purely reflex, that is they are dependent upon the mesenteric nerves to the loop remaining intact. When these are destroyed by lightly scraping the blood vessels with a sharp instrument at the time the loop is made, this important index of the filling of the loop is lost. Animals thus operated upon die rather suddenly without showing the early symptoms indicative of a high intra-loop pressure. The intoxication and the generalized peritonitis which follow rupture of the loop rapidly are fatal. This combined picture, namely, the almost immediate disappearance of toxic symptoms on relieving the distension by aspiration of the fluid and the failure of toxic symptoms to appear in a denervated distended loop until rupture occurs, furnishes strong evidence that little if any of the toxic material is absorbed so long as the mucosa remains intact.

The tendency for accumulation of fluid varies with the relative location of the loop: jejunal loops fill within twenty-four hours following the operation, ileal loops seldom fill under forty-eight hours, and seldom do colon loops show accumulation of fluid when there is no interference with the mesenteric blood supply. While the jejunal and ileal loops must be aspirated at intervals of twenty-four to forty-eight hours until complete healing has taken place, twice weekly it is advisable to wash them out by injecting and aspirating warm physiological salt solution. This prevents accumulation of a putty-like debris and thus keeps the loop in good condition for absorption experiments. We have had animals go as long as one year without their loops being aspirated and without any abnormal symptoms appearing. In such circumstances, there is a gradual filling of the loop with a putty-like substance consisting of cast-off epithelial cells, dead bacteria and salts. It will be remembered that closed loops never become sterile but carry a flora which usually is dominated by *B. coli*.

*From the Department of Physiology, University of Oregon Medical School
Submitted October 15, 1934

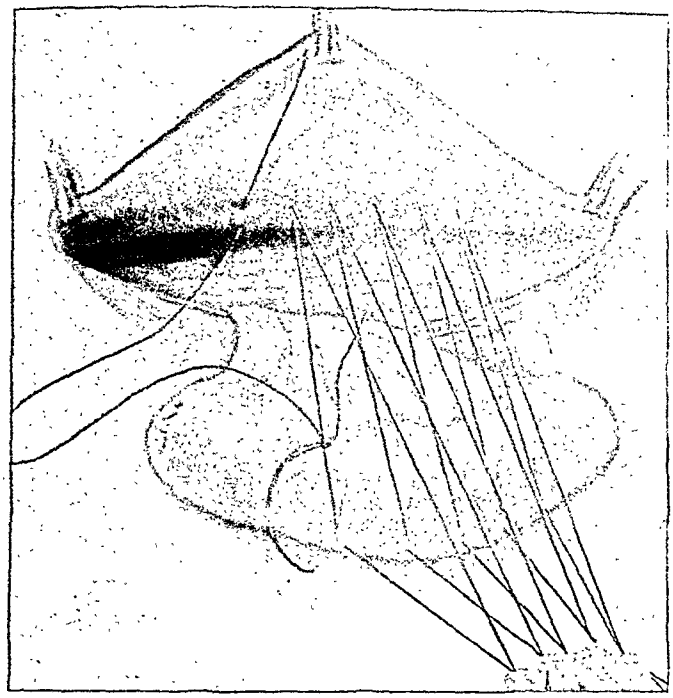


Figure 1.

Figs. 1 and 2. Method of attaching the loop to the abdominal wall so that it remains available indefinitely. Care is taken that the stitches in the serosa do not penetrate the mucosa. (Martzloff and Burget, *Arch. Surg.*, 1931, 23, p. 10.)

While colon loops require less attention and less frequent washing than do those of the small intestine, irritation of the mucosa in either will *precipitate fluid accumulation.* Repeated fluid formation following aspiration usually signifies a partial obstruction of the venous return from the loop. Before attaching the loop careful inspection is advisable in order to make sure that there has been no torsion of the mesentery while proceeding with the surgery.

Loops examined macroscopically after periods of from several months to a year were found firmly attached to the body wall and resembled in all respects segments of normal intestine. In microscopic section, the *muscularis* was found comparable with that of the intact intestine and the mucosa showed no material changes from the normal. From these observations there seemed to be no reason why these loops might not be used to study absorption.

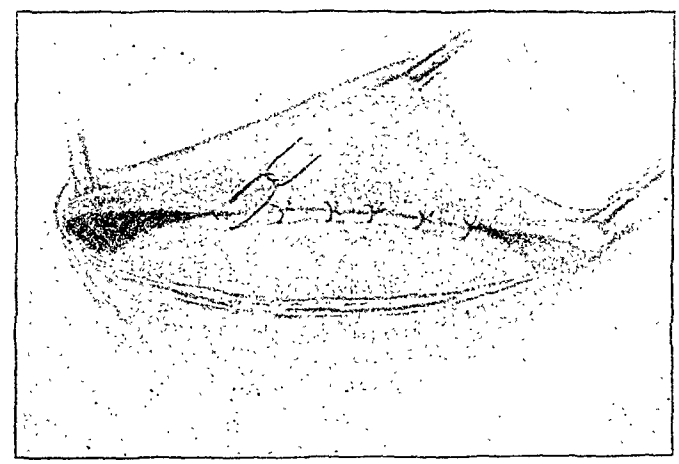
A series of experiments was carried out on the *absorption of single sugars:* dextrose, levulose, mannose and galactose.[6, 7] The animals were in good condition and no anesthetic was used. As previously stated, thrusting a hypodermic needle through the body wall into the loop caused no evidence of pain. With the animal on its back the skin over the loop is cleansed with alcohol and 10 to 20 c.c. of a solution of the sugar is injected into the loop. The animal is released and is returned to its quarters until the end of the desired interval when the loop is aspirated and washed twice by injecting small amounts of physiological saline and then aspirating. The sugar thus recovered is determined and subtracted from the amount injected in order to determine the amount absorbed. Repeated experiments on the same animal, using a constant concentration of the sugar, showed quite constant results. Of course, loops in different dogs varied somewhat in size and consequently the amount of absorption in a given time varied with the area of the mucosal surface.

The procedure is simple and is carried out on a normal, non-anesthetized animal. There need be no loss in failure to recover all the unabsorbed material since the total fluid injected into a loop may be withdrawn to within a fraction of one cubic centimeter. Washing the loop, therefore, after withdrawing the remaining fluid following an absorption interval makes for almost complete recovery of unabsorbed material. We have compared this method with the method wherein a segment of intestine is tied off in an anesthetized animal for the purpose of studying absorption. The method devised in this laboratory is much more satisfactory. Malefactors such as, anesthesia, trauma in selecting and ligating a segment of intestine, and inability to repeat the experiment in the same animal, all are obviated in our procedure.

The method of using rats by placing the solution in the stomach with a small catheter used as a stomach tube also has been compared with the closed loop. By this method the animal is sacrificed by a blow on the head at the close of the absorption interval and the stomach and small intestine carefully removed for a determination of the unabsorbed material. In order to give a sufficient quantity of sugar for a satisfactory test a high (50 per cent) concentration is used. Probably this is irritating to the mucosa and may cause reflex spasm of the pylorus thus permitting small amounts only of the solution to reach the intestine during the usual test period.

The Thiry fistula and the Thiry-Vella fistula with their various modifications have been used to study absorption. The shortcomings of these

Figure 2.



methods are so sufficiently familiar that it is not necessary to discuss them here.

The accessible closed loop method was found quite satisfactory also in answering the question as to whether or not levulose is converted to dextrose by the intestinal mucosa in the process of absorption.[3] This question arose when Bollman and Mann[4] found that levulose became less effective in combating the symptoms following nephrectomy if the intestinal tract is also removed. In order to clarify the problem, the following procedure, without sacrifice of the animal, was carried out: Forty-five minutes after injecting 10 c.c. of a 20 per cent levulose solution into the loop the animal was anesthetized and a laparotomy performed under complete asepsis. The mesenteric vessels to the loop were exposed and 10 c.c. of blood withdrawn from the vein. Systemic blood also was taken and the two samples analyzed for total sugar and for levulose. Levulose invariably was present in the mesenteric sample but never was found in the systemic blood—presumably this amount readily was taken up by the liver. The mesenteric blood sugar always was higher than was the systemic blood sugar by approximately the findings for levulose in the mesenteric blood. Thus it seemed clear that levulose is absorbed by the intestine as levulose.

Methods used for studying the absorption from the colon have been even more unsatisfactory than those applied to the small intestine. When it was found that a closed colon loop could be made and held in an accessible position indefinitely, a new method for studying the functions of the colon at once seemed available.[10] [4] These closed loops are easy to make and are less difficult to keep in good condition than are the loops of small intestine. It has been found that such loops do absorb dextrose but at a rate which is about one-half that observed in chronic loops of small intestine. The concentration of sugar giving best absorption without injury to the mucosa lay between 5 and 10 per cent. Physiological saline solution also is taken up fairly rapidly by colon loops. Sodium bicarbonate added to solutions of dextrose markedly delayed absorption of the sugar. High concentrations of salt or sugar produce considerable flow of fluid into the loop and discomfort from distension.

While these findings on the dog do not bring direct information as to the clinical value of the *nutrient enema*, yet they indicate that the colon can absorb dextrose and physiological saline solutions without difficulty. Further, they emphasize the fact, not always fully appreciated in the clinic, that high concentrations of sugar, while permitting a greater amount of sugar absorption, also cause a great influx of fluid and more or less irritation of the mucosa. These, in turn will cause discomfort to the patient and probably expulsion of the fluid with an attendant dehydration.

SUMMARY

The attachment of the accessible closed intestinal loop in dogs to the abdominal wall where it is readily entered at any time by a hypodermic needle has given evidence of the direct relationship between distension of a hollow viscus and clinical symptoms. This procedure allows for aspiration of the fluid and consequent recovery of the animal with a chronically closed segment of intestine. This closed loop adds another device for the investigation of absorption of various substances by the small intestine. It has advantages over methods now in use. The dog's colon permits the construction of a closed loop in its transverse portion.

We believe such an attached loop gives a better opportunity for studying colon function in the dog than previously has been available. It has been shown that colon loops absorb dextrose but less rapidly than do loops of the small intestine.

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The Bactericidal Power of the Stomach and Some Factors Which Influence It*

By

ARTHUR HANSZEN, M.S.
CHICAGO, ILLINOIS

IT HAS been shown by many investigators that the normal stomach is capable of exerting a powerful and quickly active bactericidal effect. As one would expect, this property seems to depend largely on the presence of free hydrochloric acid. Strange to say, however, the empty achlorhydric stomach usually is fairly sterile. Apparently some bactericidal action is exerted by the gastric mucosa.

Obviously, there are several factors which can influence the efficiency of the sterilizing mechanism. Foods which tend to bring out a large amount of acid juice should favor the destruction of bacteria. Furthermore, much should depend upon the rate with which various foods go through the stomach. As would be expected, liquids, which tend to leave the viscus rapidly, carry many bacteria into the bowel untouched by the stomach. On the other hand, solids, and especially solid foods containing much fat which tend to stay long in the stomach, are likely to be well sterilized.

Another factor which might have much to do with the sterilizing process is the buffering capacity of individual foods, that is, their ability to combine with and hold the acid. Such food will serve to hold acid in the stomach; this can be used later in the sterilization of other foods. Still another factor is the ease or difficulty with which individual foods can be acidified.

Much should depend also on the time relationships between the taking of a normal meal and the taking of infected food or fluid. For instance, a contaminated liquid put into an empty stomach probably would leave so rapidly that later the bowel might become infected, but the same fluid given at the end of a meal rich in solids might be held in the stomach sufficiently long for sterilization.

AUTHOR'S INVESTIGATIONS

The studies here described were designed to throw light on some of the conditions which hinder or help infection of the stomach and of the intestine. It is possible that work along this line eventually will supply information of considerable value, especially to persons who reside in foreign lands or to armies on the march.

*From the Department of Bacteriology and Preventive Medicine, University of Illinois, College of Medicine, and Research Laboratories of the Illinois Department of Public Health, Chicago.
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EXPERIMENTS

The experiments were carried out on seven normal persons and on many patients, most of the latter ambulant, and who were affected with minor disturbances such as hay fever. The bacterium used always was *B. prodigiosus* which was mixed with water or milk with a known buffer value and hydrogen-ion concentration. Most of the foods used to influence the sterilizing power of the stomach were fruits. Such were chosen largely because workers in the laboratory already were using these fruits for other studies on the bacteria of the intestine. Arnold has published the results of some of this work.

THE NUMBER OF ORGANISMS WHICH REACHED THE INTESTINE WHEN INFECTED WATER WAS TAKEN ON AN EMPTY STOMACH

Six apparently healthy persons each drank a glassful of tap water containing approximately 260 million *B. prodigiosus*. This water contained several hundred tiny "paraffin-wax" granules which served to delimit the stools being observed. When the stool was mixed with water, the granules floated to the surface.

After drinking infected water or milk, the person waited 15 minutes and ate breakfast. Four hours later he had lunch, and four hours later he washed out his colon with a large enema. These washings showed an abundance of the paraffin granules. Plate counts showed in four of the persons that from 9 to 27 per cent of the number of the *B. prodigiosus* swallowed were recovered. In one person, 86 per cent was recovered, and in another, 231 per cent. Obviously, in this last person, there had been multiplication of the organisms.

Unfortunately, in these experiments, the gastric acidity of the several persons experimented on was not estimated.

THE INFLUENCE OF ONE MEAL ON THE STERILIZATION OF A SECOND MEAL

In this experiment the conditions were the same as in Experiment 1, with the difference that the person ate a banana one hour before drinking the infected fluid. The result noted was that, although a large number of "paraffin-wax" granules came through, absolutely no *B. prodigiosis* could be seen.

TABLE I

Material	Cubic centimeters of normal NaOH used in titrating from pH 2.0 to pH 3.0.
Banana Dry powder 10 grams mixed with Tap water 100 c.c. 5 N HCl 2.5 c.c.	9.5
100 gm. raw banana pulp acidified to pH 2	38.0
Lemon Pure juice 25 c.c. Tap water 75 c.c. 5/N HCl 1.2 c.c.	8.0
Grapefruit Pure juice 100 c.c. 5/N HCl 1.6 c.c.	7.0
Prune Dry powder 10 grams Tap water 100 c.c. 5/N HCl 1.8 c.c.	7.0
Milk Whole sweet milk 100 c.c. 5/N HCl 1.35 c.c.	6.5
Apple Dry powder 10 grams Tap water 100 c.c. 5/N HCl 1.15 c.c.	5.5
Water Chicago tap 100 c.c. 5 N HCl 0.4 c.c.	1.5

SEVERAL FACTORS WHICH INFLUENCE THE BACTERICIDAL ACTION OF THE STOMACH

In the third series of experiments, a healthy male student was used as a subject. One and one-half hours after a test meal of milk, his gastric contents usually had a pH approximating 1.5. In the morning before breakfast, a Rehfuss tube was passed into the stomach. Then single foods of known buffer value were ingested at intervals; samples were removed and the pH determined. At intervals of from 10 minutes to two and one-half hours, food or water, infected with a known number of *B. prodigiosus* was ingested, together with the "paraffin-wax" granules to be used as a marker. Different colored granules were used on successive days. An ordinary luncheon, *uninfected*, was taken at varying periods of time after the *infected* meal. From seven to nine hours after the infected meal, two large enemas were taken, and plate counts of bacteria were made.

Experimental Series No. 3 showed that few or no bacteria reached the colon in a viable form when all of the following conditions were fulfilled. The omission of any one of them caused bacteria to come through. These conditions were:

(a) That the first or uncontaminated meal consist of a large quantity of well-buffered fruit, such as the pulp of a whole banana.

(b) That the stomach contents have an acidity greater than pH 2 just before the second or contaminated meal was consumed.

(c) That the interval of time between the first meal and the second be between twenty minutes and two hours.

(d) That the interval of time between the second or contaminated meal and the next meal be an hour or more. It appears that if a meal be taken shortly after the contaminated fluid, it is likely to wash into the stomach from the pharynx and the esophagus, bacteria which were left behind when the contaminated material was swallowed. If this third meal is large or fluid or well buffered it may carry some of the bacteria from the pharynx through into the duodenum before the stomach can become sufficiently acid to kill them. If one wait an hour before taking the third meal, the bacteria left in the pharynx all will have been washed into the stomach by saliva and then destroyed.

To sum this up, whenever conditions were such that the infected meal was promptly acidified by the remains of the previous meal, sterilization for the organism used was marked.

TABLE II

Material		Cubic centimeters of normal HCl from initial pH to pH 3.0 or "acid deficit".
Milk Whole, sweet	100 c.c.	10.0
Banana Dry powder Tap water	10 grams 100 grams	4.0
Prune Dry powder Tap water	10 grams 100 grams	3.0
Wheat cracker Dry meal Tap water	10 grams 100 grams	1.75
Apple Dry powder Tap water	10 grams 100 grams	1.25
Water Chicago tap	100 grams	0.5

THE BACTERIA ARE KILLED BEFORE THEY REACH THE DUODENUM

In these experiments, a tube was passed into the duodenum of a healthy student who had normal gastric acidity. A glass of milk infected with *B. prodigiosus* was ingested, and as was to be expected, it was found that much of this milk passed immediately into the duodenum with a pH of 7, and with no sign of sterilization. On other occasions, the milk was given one and one-half hours after the eating of two bananas. It had been shown previously by the author that these bananas soon are converted into a liquid chyme which remains in the stomach highly acid for a long period of time. In these experiments *no* viable *B. prodigiosus* could be recovered from the duodenum at any time within three hours after the taking of the infected milk. This experiment was repeated several times on ambulant patients with like results.

THE BACTERIA APPARENTLY ARE KILLED AND NOT "BENUMBED"

Because of some work done by Johnson and Arnold and by Nedzel and Arnold on the stomach of the dog, the question arose: Might it not be that the apparently dead organisms leaving the stomach are only "benumbed", and might it not be possible for them to regain their viability later? A series of experiments was performed on man by Gulbrandsen and Hood of this laboratory and by the present author, which offered no support to the view that the organisms were only "benumbed". It is a remarkable fact that if a glass of milk rich with bacteria is ingested when the stomach contains enough well-buffered and acidified material so that after mixing with the milk, the pH remains less than 3.0, viable bacteria will not be found in the fluid removed by tube five minutes later.

THE VARIED BUFFER VALUES OF DIFFERENT FOODS

In this experiment, an effort was made to find well-buffered foods which would keep the acidity of the stomach high and which would prevent the escape of bacteria following the ingestion of infected food and water. Arnold informs the author that for years physicians in the tropics have given acidified water for the prevention of cholera or have prescribed alcoholic drinks for the same purpose.

Table I shows the different buffer values for water and the foods tested. As a unit of buffer value, I have used Van Slyke's measure which is represented by the number of cubic centimeters of normal NaOH necessary to change the acidity from pH 2 to pH 3. I need not attempt here to go into the question of why one food is a better buffer than another within this particular range.

From Table I it will be seen that a number of fruits constitute very good buffers in this highly acid range. Actually, raw, acidified banana pulp appears to have a buffer value around 38, or six times that for the same weight of whole sweet milk. Furthermore, in my experiments, banana pulp gave rise to large amounts of a highly acid chyme in which much acid was held until it needed to be given off to sterilize food or water subsequently ingested.

THE AMOUNTS OF ACID REQUIRED TO ACIDIFY DIFFERENT FOODS

Table II gives an idea of another property of foods which should have a decided influence on the degree of sterilization of the stomach. This is known as the "acid deficit", or the amount of normal HCl required to change the initial pH to pH 3.

Obviously, such substances as water, which can very rapidly be brought to a high acidity, could be sterilized more easily than could milk which needs the addition of 20 times as much acid to bring it to a pH of 3. Similarly, infected bread could be acidified and sterilized more easily than could be infected bananas. Fortunately this fruit usually is sterile, bacterially, when eaten, so one does not have to be concerned over its "acid deficit".

At present, the buffer values and acid deficits of other foods are being determined, and these properties will be studied in relation to their influence on the sterilization of the stomach.

SUMMARY

It is shown that the bactericidal power of the stomach can be influenced by a number of factors. This property is enhanced by the taking of a meal one hour before the drinking of infected fluids.

Meals with a high-buffering value help to hold, and slowly give off, acid which serves to kill bacteria ingested one or more hours after the taking of a meal. In order that the bacteria be killed, it is important that the gastric contents develop an acidity as high as, or greater than, pH 2.

After drinking contaminated liquids, the taking, within a short interval of time, of another meal, perhaps well buffered and somewhat alkaline, will tend to wash living bacteria, left behind in the nasopharynx or esophagus by the infected meal, directly into the bowel.

It has been found that banana pulp serves as a well-buffered meal to hold HCl in the stomach. The buffer values of a few other foods are reported. It has been shown that the sterilization of the gastric contents can be influenced also by the resistance which some foods show to acidification, that is, the so-called "acid deficit".

ACKNOWLEDGMENT

It is a pleasure to express my appreciation of the assistance given to me by Dr. Lloyd Arnold, in whose laboratory this work was done, and also to Dr. W. C. Alvarez, Mayo Clinic, in the preparation of my material for publication.

SECTION III—*Nutrition*

A Convenient Method of Establishing Diet and Insulin Therapy in Diabetes*

By

SISTER MARY EDWINA, O.S.F., R.N.
RACINE, WISCONSIN

INTRODUCTORY REMARKS

INCESSANTLY man is seeking progress, improved methods, greater efficiency in his work. A method which requires but 48 hours for adjusting the diet and the insulin dosage in a diabetic seems a unique improvement over other methods now in vogue. Simple, concise, workable, accurate, entirely satisfactory, the method to be detailed deserves the consideration and interest of everyone concerned in this field of labor. Its chief advantages are: an immense saving of time, labor and expense; it is convenient and safe; it incurs less responsibility than do other methods and it eliminates that excessive care and worry so commonly connected with the administration of insulin.

ESTABLISHING DIET AND INSULIN THERAPY IN A DIABETIC

(a) *Study of Action of Insulin on Individual:* (1) Like others, the writer has conceived the idea that the quantitative blood sugar can be computed on a diabetic by estimating the total blood volume of the individual. Blumgarten in "Anatomy and Physiology for Nurses" states that from 1/13 to 1/12 of the total body weight is blood. The writer, because of the possibilities consequent upon insulin overdosage, has used figure 1/13. Computed on this basis, a patient whose body weight is 132 pounds should have about 11 pounds (5 kg.) of blood. Since blood sugar is expressed in terms of milligrams per 100 c.c. of blood the kilograms must be reduced to cubic centimeters. (Multiply by 1,000.) Thus one can easily determine from the blood sugar concentration, the total amount of sugar in grams in the entire volume of blood. Whether or not this sugar is present in the form of glucose remains to be proved. Judging from the amount of insulin it requires for oxidation, this sugar appears not to be a monosaccharide; or (and this seems not improbable), the product of calculation represents the number of grams of glucose in the blood stream, while the sugar in the other body fluids, kept (2) at a proportionate level with the blood concentration by osmotic pressure, plays an important role in this oxidation process. Suffice it to say here clinically we have a workable system.

By continued observation on diabetics of all kinds the writer has come to the conclusion that approximately two units of insulin are needed to oxidize every one gram of blood sugar above normal. Taking 120 mg. as normal blood sugar and repeating a blood sugar determination four hours after an injection of insulin, this conception was corroborated. Some patients were found to have blood sugar concentrations slightly above 120 mg. while those of others had dropped a little below this level. However, all were within safe limits. The patients were given no food during these four hours, but water was not prohibited. Prohibiting the intake of fluids during this period also might lessen the loss of sugar by the kidney route and thus tend to greater accuracy.

(b) *Computing the Insulin Dosage on Given Diet:* Upon this basis that the blood sugar can be controlled with some little degree of accuracy, the writer has derived another proposal, namely, that a patient's insulin dosage for a given diet can be worked out in 24 hours.

Method: A specimen of blood for sugar estimation is taken in the morning. The patient then is placed on a calculated diet consisting usualy of his requirements. Ten units of insulin once or twice a day are generally given with this diet unless one knows or suspects the patient to be only mildly diabetic. As soon as the blood sugar report is returned from the laboratory, the dose of insulin for the excess sugar in the blood is calculated. This amount of insulin, as it has nothing to do with the diet, is only given for the excess sugar in the blood. It can be given at any time but it is more convenient to add it to the mealtime dose. This also will obviate puncturing the patient's blood vessels unnecessarily. The urine is

*From the Department of Dietetics, St. Mary's Hospital, through the courtesy of Sister M. Jovita, Chief Dietitian, St. Joseph's Hospital, Milwaukee, Wis.
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collected for a quantitative sugar analysis from the time the patient takes the first meal of his diet until the following morning at 7 o'clock. At this time, blood also is again taken for a sugar test. The total sugar excreted by the kidneys, plus the excess sugar in the blood, represents the unused food of the diet. Two units of insulin for every gram of blood sugar above normal (as explained above) and one unit of insulin for the diet given and it is administered in one or more doses as the amount indicates. (We neglected to mention that if the patient has received insulin already on the first day for the diet, this quantity is to be added to the product of final calculation.)

As desugarization nearly always results in a rising insulin production and as the insulin dosage figured as above, is calculated to desugarize at once, it is well to leave a margin of safety, that is, omit about 10-15 units from the figured dose. This will safeguard the patient against an early reaction. Nevertheless the patient is given full instructions concerning the use of insulin, insulin reactions both hypoglycemic and allergic, also regarding the urine sugar test and the diet. As a special aid to the patient at home he is provided with a sheet containing the following instructions:

SPECIAL INSTRUCTIONS TO PATIENTS

It is of the utmost importance that insulin be taken regularly at the appointed time.

If symptoms of an overdose or reaction (unusual hunger, trembling sensation, profuse perspiration, in some cases blurred vision) occur, take a small amount of food or a teaspoon or two of sugar in water *immediately*. This may be repeated in thirty minutes if necessary.

Do not become alarmed about insulin reactions. They would seem to give proof that your own pancreas is making more insulin. Therefore when you get a reaction (but it must really be one) you may reduce your insulin five units per day, or, ten units, if the reaction was very marked. This may be done after each successive reaction. Insulin reactions may occur after a patient is on treatment for a long time, or, they may occur very early in the course of treatment. And usually they produce improvement in the patient, a reward which comes to nearly all who faithfully adhere to their regulations.

All diet regulations are individual in character. Every diabetic must consequently follow exactly the instructions given him or her and pay no attention to what others do. If you feel strong enough to do your customary work and are maintaining your normal weight, your diet should be considered adequate. Should your diet for any reason seem inadequate or unsatisfactory, do not change it yourself, but consult your doctor or a dietition, as the case may be. The diet and insulin are always carefully adjusted; hence it would be unwise, not so say dangerous, to shift around or change the diet. From what has been said, naturally it follows that if one is provented from taking the usual amount of food, the insulin must be omitted proportionately. Also when the taking of a meal is deferred, if insulin is prescribed for that meal, it must be taken later likewise.

Ordinarily, it suffices to examine the urine, usually a morning specimen, about twice a week. A sugar-free urine is *no indication* to reduce the dose of insulin. When you find sugar in the urine add two or three units of insulin each successive day to the regular dose until the urine again becomes sugar-free and then continue on that dose till such a time when your condition would suggest a reduction as described above. A large amount of sugar in the urine (indicated by the number of drops of urine it takes to reduce the testing solution), if not brought on knowingly by a deviation from your regimen, and if it does not readily yield to larger doses of insulin, may indicate that you need immediate medical attention.

In spite of the fact that things may be running smoothly it is advisable to have a blood sugar test made once or twice a year.

It is all-important that you understand everything pertaining to your treatment very thoroughly. If you are in doubt about anything, come back for further instruction.

KEY TO URINE TEST FOR SUGAR

Number of drops of urine indicate amount of sugar present—

From 1- 5 drops, a very large amount.
From 5-10 drops, a moderately large amount.
From 10-15 drops, a small amount.
From 15-20 drops, a trace.

N.B. Insulin reactions may occur as late as four to five hours after the injection, rarely later than that.

ACIDOSIS

Computing the dose of insulin from the quantitative blood sugar is of appreciable value in treating patients who exhibit acidosis. The calculated amount of insulin may be given without a buffer. Any subsequent insulin, however, must be buffered with some form of carbohydrate. Apparently all diabetics in coma or in a comatose condition are complete diabetics having no sugar tolerance whatever. This condition of a non-functioning pancreas may be either temporary or permanent. In such a state, the patient can hardly utilize more than one gram of sugar for every unit of insulin given. Still it is safer to allow a small surplus of sugar until by studious observation one has ascertained the patient's tolerance. The writer frequently uses one and one-third grams of sugar to one unit of insulin. These proportions are conveniently safe and obviate the necessity of frequently repeated laboratory tests.

The method of computing the blood volume and insulin dosage follows in detail: In case of coma one must estimate the patient's weight or, if possible, ask it of relatives. In estimating it, it is better to aim rather too low than too high, as treatment based upon a weight estimated too high might lead to an overdose of insulin.

Computation: Example—1/12 of body weight, 172 pounds, equals 14.33 pounds blood; 14.33 divided by 2.2. equals 6.5 kg., or 6,500 c.c. blood: 400 mg. minus 120 mg. equals 280 mg. excess sugar in every 100 c.c. 6,500 divided by 100 equals 65, and if there are 280 mg. excess sugar in every 100 c.c. of blood, then, in the total volume there will be 280 times 65, which is 18,200 milligrams. The insulin is adjusted to grams: therefore, milligrams must be converted to grams. This is done by dividing by 1,000 or, simply by pointing off three places to left—18.200 divided by 1,000 equals 18.2 gms., total blood sugar: hence, 18 times 2 equals 36 units of insulin needed to oxidize this.

SPECIAL REMARKS AND CAUTIONS

There is a class of severe diabetics, which we like to call "complete diabetics", but if a complete diabetic is one whose pancreas has ceased

functioning entirely, then these patients are not all complete diabetics. The principal characteristics of these patients is a persistent, high blood sugar and a 4-plus urinary sugar finding in the morning. This accumulation of endogenous sugar cannot be prevented except by giving insulin through the night. However, this procedure is not recommended. Because of the accumulation of sugar overnight, these patients need their largest dose of insulin in the morning but only just enough to take care of their food at the other two meals. In this way, these patients can be kept at a fairly normal level throughout the day and part of evening. In severe instances of diabetes, some doctors recommend giving a moderate dose of insulin with a lunch at about 8 or 9 P. M. Since these patients never are sugar free in the morning, the best time to check up on them (both blood and urine tests) is between five and six in the evening—when the noon dose of insulin has exhausted its action and before the supper dose is given. At this time patients should be found nearly normal if the diet and insulin are well adjusted.

How can one recognize these cases?

The very severe case easily is recognized by the result of the 24-hour quantitative estimation of sugar where the output will be found to be greater than was the sugar intake in the diet. The moderately severe case, on the other hand, presents rather more difficulty. While his output of sugar is very large, it does not exceed his intake. One is unable to say immediately whether or not a part of this sugar has its source in an over-night endogenous production, or whether it represents simply unused food waste. If the day's insulin evenly is distributed in proportion to the meals, insulin reactions in the afternoon and evening probably will lead one to suspect the situation. By careful observation and the finding of abundant sugar in the morning specimens, both blood and urine, one soon may place him in the category to which he belongs.

The important and difficult requirements in both these types of patients is to get the insulin properly adjusted. The calculation of insulin dosage for the excess sugar in the blood always holds, for all cases alike; but in the above-mentioned types of patients the figure for the urine sugar—one unit of insulin for each gram of sugar—does not hold. In such circumstances it will take rather longer to adjust these patients. However, such instances are not numerous.

CONCLUSION

The above outlined method of establishing diet and insulin therapy in a diabetic is direct and has proved to be reliable. Since it is a purely mathematical procedure, it should produce the same happy results in the hands of the inexperienced and timid worker as it does in those of experienced doctor or specialist.

NOTE: It is interesting to observe the action of insulin on different individuals. This study of the variable action of insulin was the beginning or first step in working out the above method; but readily one may see that it is not necessary to do this on every individual. To omit it saves much time and expense. When individualized action studies are done they must be carried out on a separate day.

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Studies in Food Allergy* . . . A Preliminary Report

By

ANTON W. OELGOETZ, M.D.; PAUL A. OELGOETZ, B.A. (Chem.)

and

JUANITA WITTEKIND, R.N.

COLUMBUS, OHIO

THE whole subject of food allergy practically has developed into a big question mark. According to Vaughan and others, who have had large experience (1), skin tests are not more than 50 per cent reliable. This investigator states that of 200 positive skin tests to foods, only 100 of the foods actually were causing trouble. The other half were "false" positives, or at least, were not responsible for disturbances. For every 100 foods actually found to be factors influencing symptoms or signs by the skin-testing method, 40 additional foods were found to be inimical agents by the method of keeping food "diaries" or by "elimination" diets; yet these foods returned negative skin tests.

It is difficult for the authors to believe that any

*EDITORIAL NOTE: Inasmuch as both clinical and investigative aspects of food "allergy" are in a confused state and because progress along so-called orthodox lines appears to have reached an impasse, on the basis of its offering suggestions along different pathways, this article has been deemed worthy of publication. It is a "preliminary report". The data presented may find elaboration by those interested in the problems discussed. Be that as it may, such work, performed by men busy with everyday practice, warrants recognition.

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test which in the hands of experts admittedly is 50 per cent unreliable can be regarded in any special instance as a dependable specific procedure. Every doctor who has worked in the field of allergy has known patients who were sensitive by skin tests to certain foods at one sitting, and were negative to the same foods a week later. Plainly, the skin test does not have the same specific significance in food allergy as does an increased lipoid content of the serum in syphilis, upon which the sero-diagnosis of that infection depends.

Likewise, the leucopenic index (e. g., "Widal crisis") as an indication of allergy, according to Vaughan is only 67 per cent correct, and the method has the further disadvantage of being too time-consuming for routine use. Food "diary" and "elimination" diets look well on paper but in our hands they have proved impracticable. Just about the time one seems about to gain information by this method, the patient is called out of town, where he must eat at restaurants which breaks, unavoidably, the entire planned regimé.

It would seem that the reason why so much confusion has existed in the field of allergy is that, etiologically, there are different types of allergy just as there are different types of infection. Perhaps the underlying mechanism is different for each type. There is evidence that food sensitization essentially is a pancreatic disturbance, as we shall attempt to show, while allergy to pollens, bacteria and other allergens probably depends upon an entirely different mechanism. In this study we are concerned only with sensitization to foodstuffs. We believe that we have uncovered some very pertinent data.

It has been advanced that sensitization to foods is a form of anaphylaxia. In animals, only the injection of whole, soluble, undigested proteins will produce sensitization. Split products of digestion will not produce sensitization. It is believed that sensitization results from the formation of specific antibodies, and that it is the union of large amounts of antibody with its specific antigen which is the cause of the chemical "explosion" which we call anaphylaxia. Some workers claim to have demonstrated antibodies in the serum of sensitive animals but a greater number were unable to confirm these findings. Our impression derived from the literature is that antibodies never have been surely and definitely demonstrated. For a full exposition of our present knowledge the reader is referred to any of the standard texts on the subject, such as Vaughan (2), Tice (3) or Kolmer (4).

DISCUSSION OF METHODS AND RESULTS

Because antibodies are specific substances formed as a result of specific allergens gaining entrance to the blood stream, we have worked with allergens which were extracted from the various foodstuffs in the forms in which commonly they are eaten. Beef, for example, usually is taken in the cooked state, while apples are usually eaten in the raw state. We prepared beef antigen by extracting finely chopped beef with saline solution. The beef was cooked in the saline solution for two hours, after which the solution was filtered and neutralized for free acidity. Those foods which are commonly eaten in the uncooked state were extracted with cold saline for 24 hours, after which the saline was decanted, filtered and neutralized.

Allergens made in this manner were studied by means of Weichardt's epiphanin reaction (5). Weichardt found that if a solution containing soluble protein is introduced into a "system" composed of a balanced mixture of sulphuric acid and barium hydroxide, plus phenolphthalein as an indicator, the protein alters the surface tension of the finely divided barium sulphate particles by its colloidal action, so as to increase the absorption of H or OH ions, depending on whether or not the protein is fixed or free.

Weichardt's reaction is dependent upon physico-chemical properties of absorption and it acts in accordance with the following generalizations: (6) Solutions containing colloids (proteins) *i. e.*, antigen alone, serum alone, or antigen plus nonspecific serum, act in the epiphanin system by shifting the phenolphthalein endpoint in the sense of absorbing OH ions, thus liberating H ions and making the solution more acid (less red). When free proteins are added to the epiphanin system, the system becomes less red (more acid). On the other hand, solutions containing an antigen plus its specific antibody do not produce a change in the epiphanin system, as the antigen and its specific antibody fix each other. This reaction is very clean-cut and definite; the strength of any solution containing free protein accurately can be titrated and the presence or absence of specific antibodies determined.

By studying the cooked antigens prepared as above, by means of this system, we found that they did contain free, soluble protein, but never were we able to demonstrate the presence of specific antibodies in the serum of sensitive rabbits. That the rabbits were sensitive was proved in that they all showed the phenomenon of Arthus after daily intraperitoneal injections of 2 c.c.; when larger doses were given (5 c.c.) the animals showed all of the signs of protracted anaphylaxis.

Serum from these rabbits also was tested by a technique similar to the Kahn and the Meinicke tests for syphilis, with negative results. Antibodies could not be demonstrated by means of the complement-fixation test. Neither could precipitins be demonstrated with any regularity. Therefore, we concluded that injected, *cooked* allergens (the form in which they must sensitize people if they do so at all) do not provoke the formation of specific antibodies, and that allergy to foods is not caused by the union of antigen and its specific antibody.

However, it was noted that when rabbits were injected with any of the cooked antigens, some

substance appeared in the serum which caused a greatly increased shift in the epiphanin system. For example, if the serum taken from a rabbit before it had been injected (non-sensitive) was titrated by means of the epiphanin system, the serum usually would show an endpoint in a dilution of approximately 1-80. Two weeks later, after having received daily intraperitoneal injections (2 c.c.) of any antigen, serum from the same rabbit would show an endpoint in a dilution of 1-2500. Plainly something was changing in that blood.

Another interesting phenomenon also was noted in this connection. If a sensitive rabbit was titrated on the same day on which the serum was taken, we would, for example, find a titration endpoint of 1-2500. If this same serum were permitted to stand in the icebox overnight, the activity of the serum in the epiphanin system would drop to 1-320. Then, if the same serum were titrated 24 hours later, it would be back to normal, *viz.*, 1-80. In short, the agent which was causing the shift in the epiphanin system was extremely labile; heating to 50 degrees C. for 30 minutes caused the substance to disappear entirely.

On the supposition that this unknown substance or agent might be an enzyme (one of Abderhalden's "protective" enzymes) we tested the sera of sensitive rabbits with 5 per cent suspension of starch and iodine, and with a ½ per cent solution of albumin. One cubic centimeter of the starch suspension was added to each of six tubes. The first tube received .05 c.c. of pure serum; the second, 0.1 c.c.; the third, 0.2 c.c., and so on. Similar tubes were set up containing varying quantities of protein (albumin) and olive oil. In this manner we demonstrated in the serum a substance or agent which in a dose of .05 c.c. of pure serum was able completely to digest the standard testing solutions in 24 hours. Normal rabbit serum also was found to contain this agent, causing complete digestion in a dose of 0.1 c.c. of a 1-10 dilution. Normal human serum was found to contain this agent, causing complete digestion in a dose of 0.2 c.c. of pure serum. Rabbit serum, therefore, would appear to contain more of this pancreatic-enzyme-like substance than does human serum.

The serum of sensitized rabbits next was tested against the cooked antigens and it was found that digestion took place in the same dosage as was found effective against the starch and albumin mixtures. The reaction was found to be non-specific. the serum digesting any protein equally well. We concluded from the above experiments that normal rabbit serum contains an amylase-like agent which hydrolyzes starch to sugar, a trypsin-like agent which racemizes all proteins, and a fat-splitting agent. These "enzymes" are found in the sera of all normal animals in a remarkably constant concentration.

BLOOD SERUM TEST FOR ENZYME ACTION

Subsequently, we made a study of a large number of human sera. It was found that normal human sera always contain these enzymes in a concentration which is so constant that their determination can be used as a specific test. If 0.2 c.c. of pure human serum is added to a tube containing 1 c.c. of 5 per cent starch-iodine suspension, complete digestion will take place in 24 hours, when incubated at body temperature.

During the course of these experiments it was further learned that enzymes do not always act as catalyzers, merely accelerating a reaction as oil facilitates the running of a machine, the enzyme itself not appearing in the end-product; but that they are "bound" or fixed chemically by the substance upon which they act. A given quantity will digest completely the testing solution; a lesser quantity will not cause complete digestion no matter how long it is incubated.

Because three enzymes would appear always to be found in normal sera, and because they acted exactly like the pancreatic enzymes, splitting proteins, carbohydrates and fats, and because they did not exhibit a specific action, digesting all food substances equally well, we concluded that the serum enzymes were in fact pancreatic-like enzymes which had been absorbed—free—into the blood stream. And because these enzymes are found in all normal human sera in a concentration in which 0.2 c.c. of pure serum will digest completely 1 c.c. of the standard starch mixture in 24 hours, we concluded that an agent acting like free pancreatic juice in the above concentration is a normal constituent of human serum. In fact, it may be pancreatic juice.

Our observations are in accordance with those of Boldyreff and his workers at Battle Creek (7). Long ago they demonstrated that the pancreas periodically secretes pancreatic juice, rich in enzymes, into the duodenum from whence it is absorbed into the blood where it can be demonstrated. The Abderhalden reaction depends upon these free pancreatic enzymes and not upon specific, protective enzymes as Abderhalden believed; this is the reason why the test has been found to be non-specific as a test for pregnancy.

Our findings (arrived at independently) differ from those of Boldyreff in one important respect. Boldyreff claims that the pancreatic enzymes are secreted periodically throughout the day, and that there are times during the day when the enzymes completely disappear from the blood. This has not been our experience. We have never encountered an instance in which the normal concentration could not be demonstrated.

SIGNIFICANCE OF BLOOD SERUM TESTS FOR "ENZYMES IN RELATION TO NUTRITION"

If a normal individual, one who has no difficulty with any type of food in any quantity, whose weight is normal and whose blood contains the normal complement of free enzymes, is given a diet in which the quantity of protein, carbohydrate and fat is greatly increased, the blood will still show the same concentration of free enzymes.

However, if one observes an underweight individual, one who is habitually underweight and in whom no amount of food will cause a weight increase, there is a different situation. On his normal diet (which, however, is insufficient to maintain normal weight) such an individual will show the normal quantitative values for free serum enzymes. But if his diet is increased, the enzymes will disappear from his blood. Inasmuch as the blood is taken from the patient at the same hour each day, this disappearance of the enzymes cannot be due to the periodic disappearance of "enzymes" as claimed by Boldyreff.

In short, normally as a result of the stimulation of food intake, the pancreas may be considered to secrete a sufficient quantity of enzymes to unite with all of the food taken, plus an excess—which it seems may be absorbed free into the blood stream. This is in accordance with the findings of Boldyreff. But the underweight individual appears to be unable to secrete sufficient enzymes to digest even a ration which will maintain his normal weight. If he is given an increased ration, he is unable to digest all of the food, perhaps because an insufficient quantity of enzymes is present; because the food fixes all of the enzymes, no free enzymes pass into the blood stream and the normal serum enzymes disappear from the blood. From the concentration of enzymes in the serum of an individual on his regular ration and after taking a test meal consisting of a greatly increased ration, it appears that the serum taken at the same hour each day, may be regarded as a direct measure of that individual's pancreatic function.

All the chief pancreatic ferments—those splitting carbohydrates, proteins and fats—are being secreted by the secretory cells of the pancreas at the same time and are inseparable in the pancreatic juice. Some physiologists believe that they form one common chemical molecule. This may explain why protein, carbohydrate and fat metabolism is affected if any of the enzymes are affected (8). This is in accordance with our findings; the concentration of all of the pancreatic enzymes always was found in the same relative proportions. If any of them were present, they were all present in the same relative concentration. When the concentration of amylase decreased, they all decreased. We have used this observation to simplify the technique of our test. Instead of testing for the presence of all three of the pancreatic enzymes, we have simplified the procedure by testing for amylase alone. Practically, the test is performed as follows:

APPLICATION OF THE SERUM TEST FOR ENZYMES

The first day the patient reports at a given hour and his blood is taken. In about two hours, or just so soon as the serum separates from the clot, it is centrifuged free from cells and three tubes are set up. Tube one is the control; it receives 1 c.c of the standard starch-iodine suspension; tube two receives 1 c.c. of the starch-iodine suspension plus .05 c.c. of pure serum; tube three receives 1 c.c. of the starch-iodine suspension plus 0.1 c.c. pure serum. The tubes are incubated at body temperature for 24 hours. Tube one, of course, never shows any change. Tube two, in a normal individual, usually shows almost, but not quite, complete digestion. Tube three usually shows complete digestion.

The patient is then instructed to double his regular ration. If he has been in the habit of eating one egg for breakfast, he takes two; if he has been eating two pieces of toast, he is instructed to eat four pieces, and so on. We make no effort to place him on a definitely increased diet, containing a definite increase in the caloric value, but simply to have him definitely increase the normal food intake. He reports at the same hour the next day at which time again his serum is taken. This time, however, we set up eight tubes. Tube one is again the control; successive tubes contain .05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6 c.c. of pure serum. The tubes again are incubated and are read in 24 hours. If the individual's serum will digest all of the testing solution *completely* in a dose of 0.1 c.c. the first day and will repeat the response on the second day, we assume that his "pancreatic threshold", or response is normal. On the other hand, if complete digestion takes place with 0.1 c.c. the first day, while it requires 0.6 c.c. for complete digestion the second day, the difference between 0.1 and 0.6, *viz.*, 0.5, we regard as a direct measure of pancreatic inability or hypofunction.

SIGNIFICANCE OF BLOOD SERUM ENZYME DEFICIENCY IN ALLERGIC SUBJECTS

If underweight individuals who are unable to maintain the normal concentration of blood enzymes on the test ration are continued on the increased ration for several days, invariably they show evidences of food sensitization. They report herpes, pimples, canker sores and various indefinite digestive disturbances. If now they are given pancreatic enzymes (dry and enteric coated so as to be liberated in the duodenum) or the total food intake be reduced, the evidence of sensitization disappears. No longer do they complain of indigestion. They begin to increase in weight and the free enzymes again appear in the serum in normal concentration. This observation has led to a *present* conception of food sensitization which we summarize as follows:

In a normal individual (in whom a normal quantity of enzymes can be demonstrated in the blood serum) the pancreas secretes enzymes as a result of the stimulation of food sufficient to combine with *all* of the food taken, plus an *excess* which passes "free" into the blood. The normal serum-enzymes are an excess over and above the digestive requirements. They pass into the blood where it would seem they serve a protective function, acting as a "buffer solution", combining with any free food which has passed into the circula-

tion. Boldyreff is of the opinion that finally they are also absorbed by the body cells where they continue the digestive processes and thus maintain normal metabolism.

If such an individual overeats (takes our overfeeding test meal) the pancreas would seem to be stimulated to a greater degree and responds with a greater quantity of pancreatic juice, thereby producing sufficient enzymes for all of the food needs and adequate to maintain the normal "buffer" solution in the blood. In our experience, such an individual can maintain his normal weight, handle almost any quantity of food and never will become allergic.

On the other hand, the individual who has inherited (?) a poorly functioning pancreas, or whose glandular functions temporarily are depressed by reason of disease, gets into trouble when he surpasses the normal secretory threshold of his pancreas. If such an individual takes more food than can be digested, free protein passes into the blood. And because no excess enzymes have been secreted or are available, the buffer enzymes are absent and the protein continues to circulate as free protein which cannot be further split. Meanwhile in such abnormal situation it exerts its own physiological action which is essentially that of chemical irritation. Pure pancreatic juice is exceedingly irritating (8). It may be that the tissues are in this process sensitized, by reason of the free protein. From such anomaly, we believe that "sensitization" to foodstuffs results.

There has been some question as to whether whole, unracemized proteins ever enter the blood stream. When protein reaches the stomach, it meets HCl and pepsin which change part of it to acid metaprotein. Acid metaprotein is soluble and immediately may be absorbed into the blood stream. The food then passes into the duodenum where it encounters alkaline secretions which change any unchanged protein to alkali-metaprotein. Alkali-metaprotein likewise is soluble. Acid and alkali-metaproteins are normal constituents of blood serum, following meals. (One of us, P. A. O.)

Therefore, proteins are not always changed to amino-acids in the bowel; indeed, the greater part of digestion may be carried to completion in the blood stream. The blood, therefore, may be regarded as a more important final "digestive organ" than is the gastro-intestinal tract. Of course, the process is a continuous one; while a portion of the ingested protein is being absorbed into the blood as acid or alkali metaprotein, combined with pancreatic enzymes, the enzymes are acting upon another portion, changing it to proteoses, peptones and finally to amino-acids. The point we wish to make clear is that the gastro-intestinal tract essentially is a receiving and mixing organ where the food is mixed with acid or alkali and enzymes; because the metaproteins are soluble, it is our theory that the greater part of digestion takes place in the blood stream, and according to Boldyreff, finally in the body cells themselves.

In some respects, this observation is in accordance with the investigations of Walzer and his associates (10). Walzer obtained serum from a case very strongly allergic to fish and injected it into the skin of a non-allergic recipient, thereby rendering a portion of the skin passively sensitive to fish. The recipient then ate the fish in question and in a short time urticarial wheels appeared at the site of transfer. This experiment was repeated and the result again produced in a subject sensitive to eggs. Such observations prove that egg and fish protein normally are absorbed into the systematic circulation and carried through the blood to the site of transfer, still sufficiently unchanged as to be identified by a specific biologic reaction.

Most proteins consist of two parts: a protein nucleus which is common to all proteins, plus the addition of some other molecule. Such construction explains why all proteins are digested by the same enzyme, accounts for the biologic reactions manifested in skin tests, and it is the presence of the prosthetic group (not the protein nucleus) which results in the irritation of the body cells ("shock organs") a response which we know as sensitization. If the prosthetic group in the protein molecule is the cause of the specific biologic reaction and not the protein molecule, then one would expect to get positive skin tests in the case of compound proteins, while simple proteins would give a negative reaction. We are now working on this phase of the problem and later hope to have something to report.

Because metaproteins are soluble, part of the ingested protein passes into the blood stream before it has combined with the pancreatic enzymes, and we believe that it is the function of the buffer enzymes in the blood to "fix" and digest these free proteins. If buffer enzymes are not present, by reason of a hypo-functioning pancreas, the uncombined proteins continue to circulate as free proteins, apparently irritating all of the cells of the body. Then one observes what is called sensitization or allergy. Why these blood proteins irritate some tissues (shock organs) more than others still is unknown.

Because pancreatic enzymes do not exert a specific action, but will digest all proteins equally well, allergy results, not from an *excess of any one* specific protein, but from a *general excessive food* intake. Thus, treatment consists of a general reduction of the total caloric intake. If a total reduction within the limit of the pancreatic threshold still will permit normal weight, then no other treatment is necessary; but if the pancreatic threshold will not permit normal weight, then it becomes necessary to give as it were our horse help by introducing another horse into the team. Such help may follow the giving of dry pancreatic enzyme in sufficient quantity to maintain nor-

mal weight and to maintain the normal complement of serum enzymes.

It has been common clinical practice to test for the pancreatic enzymes in the duodenal secretions. Most men no longer perform these tests as rarely are the enzymes found to be absent. But according to the above work (and that of Boldyreff) to test for pancreatic enzymes in the duodenal secretions is not a rational procedure. The question is not whether an individual has *any* enzymes present, but how *much!* Does he have enough? The test must be quantitative, not qualitative. Merely to make a qualitative test for enzymes in the duodenal secretions is equivalent to testing the blood for hemoglobin to determine anemia. We know that hemoglobin always is present in blood; what we wish to know is *how much* is present. The only manner in which one can determine the quantity of pancreatic enzymes which is being secreted is by determining the blood serum enzymes. If sufficient pancreatic enzyme has been secreted to combine with all the food taken and to provide the buffer solution in the blood, then we know that that patient's pancreas is functioning normally. If that same patient is given the overfeeding test diet, a greatly increased ration, and the buffer enzymes still appear in the blood in normal concentration, then we know that the pancreas is equal to all demands. He is not sensitive to any food and he can maintain a normal weight. We think that a determination of the circulating enzymes, therefore, is the logical test for pancreatic efficiency, digestion and allergy.

Assuming this theory to be correct, then one should be able to explain every phase of allergy. A common example of allergy to foods is urticaria. Ordinarily a dose of salts, which relieves the bowels of excess food, and a reduced diet for a day, is all the treatment required.

From our viewpoint, the mechanism of acute urticaria is as follows: Our patient eats an excess of food. The undigested portion of starch and fat, being insoluble, remains in the gastrointestinal tract where it is the cause of gas and fermentative processes. In the stomach, part of the protein is changed to metaprotein and is absorbed. In the duodenum the remainder is changed to alkali-metaprotein, combines with the pancreatic enzymes present, and then gradually is absorbed into the blood stream; then the protein gradually is split through the various stages of derived proteins to amino-acids.

But because there occurred an insufficient quantity of pancreatic enzymes (when the patient's food intake surpassed his pancreatic threshold) part of the metaprotein passes free, uncombined with enzymes, into the blood. For the same reason (pancreatic hypofunction) the buffer enzymes are absent from the blood and the free uncombined metaproteins remain unchanged in the circulation. Meanwhile the patient has purged himself, placed himself on a limited diet which permits the pancreas to catch up, as it were, the buffer enzymes are restored, the free metaproteins in the blood are digested and there occurs spontaneous recovery.

On the other hand, a patient who habitually surpasses his pancreatic threshold, especially in the realm of his usual diet (staple foods) never "catches up". Because the circulating metaproteins are not digested, they continue to irritate the tissues, perhaps forming loose compounds with the body cells, which, because such compounds are unphysiological, are poisonous. This is a supposition, a working of hypothesis and has not been proved; it requires further study. However, Walzer's observations would seem to indicate that some such mechanism is at work in the phenomenon which we call sensitization.

Treatment of this type of patient consists of a reduction in the total food intake. If the subject can maintain his normal weight on the reduced ration, no other treatment is necessary. If he is unable to maintain his normal weight, in addition to the buffer enzymes in the serum on the reduced ration, assistance may be secured from dry pancreatic enzymes administered to augment the normal but, in such patient, deficient pancreatic function.

Allergy or sensitization to foodstuffs, explained on the above bases, therefore, is not a pathological condition but a pathological exaggeration of a normal physiological mechanism. The above data explain why 60 per cent of the population have allergic manifestations at some time in their lives, and why most of such instances may be acute but, usually, clear up spontaneously. This conception would seem to indicate that inheritance has nothing to do with the allergic state except inasmuch as one may or may not inherit a functionally adequate pancreas. All that is necessary for the appearance of the allergic state is that one be exposed to massive doses of food, a quantity of food sufficient to surpass the individual pancreatic threshold at a particular time or constantly.

The above data would seem to explain why allergy to foods practically is unknown in the Orient. Because of the low scale of living, probably the Oriental rarely gets sufficient food to exceed his needs, *viz.*, surpass his pancreatic threshold. They also explain why acute allergy commonly clears up without treatment, and why many people lose their sensitizations after prolonged avoidance of proteins (although it would appear that it is the *total* reduction of food which acts beneficially and not the elimination of *any specific* protein), and why many patients can maintain a state of "allergic balance" by continual dietary restriction.

Our data and our theory seem to explain why allergic individuals usually are sensitive to foods with which they come into continuous contact. It follows that, if one only eats oysters occasionally, it would be difficult for this protein to cause trouble. Sensitization is more likely to follow the ingestion of such staples as beans, bread, eggs, meats, milk. If one exceeds the pancreatic thresh-

old, naturally he will do so in the realm of these staples; because they *are* staples in the average dietary they are more likely to produce chronic sensitization. Our theory also explains the uniform lack of success following desensitization in food-sensitive individuals. Desensitization fails because allergy is not caused by any *one* foodstuff, but on the basis of total food intake being too large for the individual.

Sensitization to foods is the most frequently noted manifestation of clinical hypersensitiveness (allergy). It does not always manifest itself as a definite disease syndrome, such as asthma, but commonly causes minor symptoms, as headache, "indigestion" (which cannot be accounted for on an organic basis), canker sores (which refuse to depart until the underlying pancreatic secretory deficiency is corrected), "pimples" (not acne), herpetic eruptions and the like.

SUMMARY

1. Most of the protein ingested is not split to the stage of amino-acids in the gastro-intestinal tract. A large part of the protein is absorbed into the blood as acid or alkali metaprotein and other derived proteins. The gastro-intestinal tract essentially is a receiving and mixing mechanism. Digestion is started in the gastro-intestinal tract but is continued and completed in the blood stream.

2. Normally, sufficient pancreatic juice is secreted to combine with all of the food eaten and to provide an excess which passes free (uncombined) into the blood stream, where it acts as a buffer solution, combining with and digesting any food which has been absorbed unmixed with enzymes.

3. Blood serum normally contains free pancreatic enzymes in a definite and constant concentration. These enzymes can be demonstrated by a simple test which we have described.

4. The concentration of pancreatic enzymes in the blood serum of an individual on a regular ration, compared with that after taking a "test meal" consisting of quantitatively a greatly increased total ration, appears to be a direct measure of that individual's pancreatic (digestive) function.

5. It is probable that "hypersensitiveness" to foods is caused by an excess of free food (free of enzymes) in the blood serum, and that this excess is caused by a low pancreatic threshold (hypofunction).

6. In our opinion, the state of "allergy" to foodstuffs can be determined by ascertaining the concentration of free amylase in the serum before and after a test meal.

7. The rational treatment of sensitization to foods lies in the reduction of the total food intake. If the patient can maintain normal weight and adequate buffer enzymes on the reduced ration, no other treatment is necessary. If he is unable to do so, it would seem that dry pancreatic enzymes must be administered to make up the shortage.

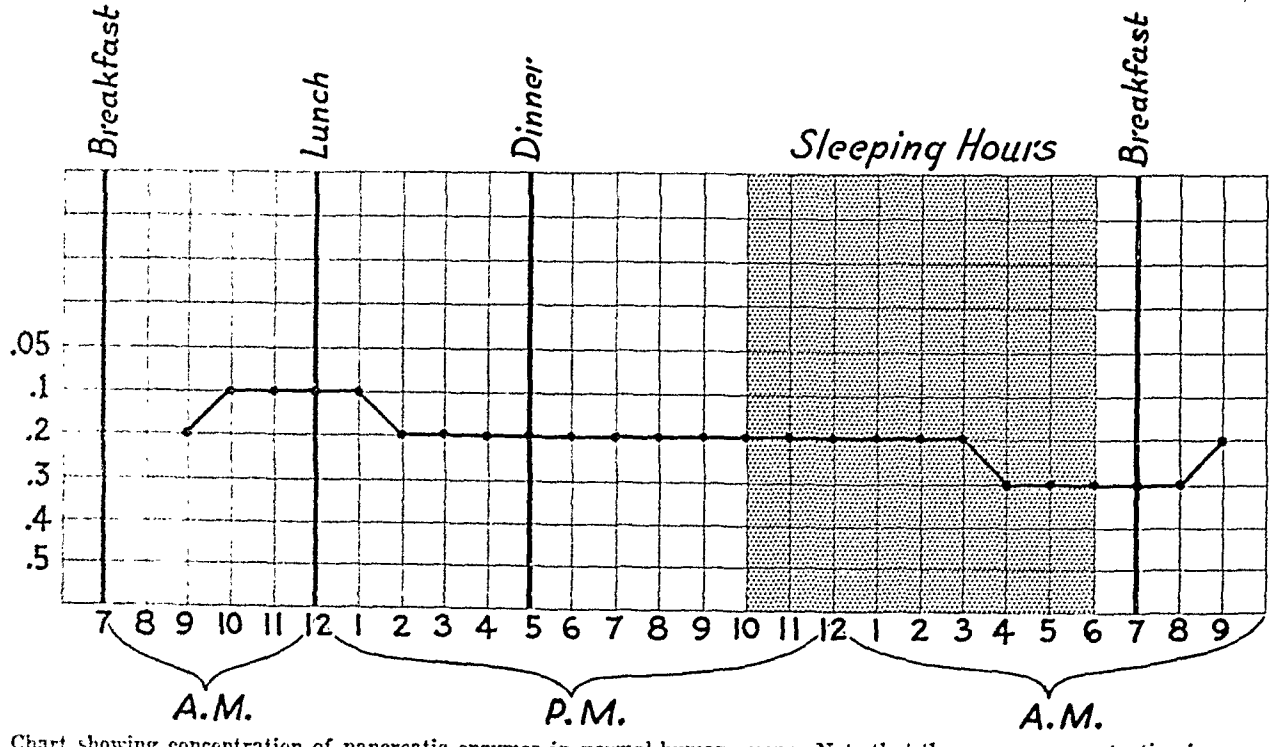


Chart showing concentration of pancreatic enzymes in normal human serum. Note that the enzyme concentration is practically constant throughout the 24-hour period. Food intake and sleep (empty stomach) have no influence on concentration of enzymes in normal human serum, the enzymes passing into the blood steadily and in a practically constant concentration. The slight rise after breakfast and the slight fall at 4 A. M. are of no significance. (.05, 0.1, 0.2, 0.3, 0.4, 0.5 c.c. were the quantities of pure serum used in the tests. The serum was tested against a standard 5 per cent starch-iodine suspension, which was incubated for 24 hours at body temperature.)

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ABSTRACTS

CHARLES M. BLUMENFELD.

Endocrinology. Weight Changes in the Suprarenal Glands of Albino Rats on Vitamin E Deficient and Fat Deficient Diets. 18:367-381, May-June, 1934.

Blumenfeld has demonstrated a relationship of the suprarenal to vitamin E and to fat metabolism. Rats deprived of vitamin E and killed during the second pregnancy had suprarenals, the cortex of which was questionably hypertrophied, but the medulla of which was definitely atrophied. Rats maintained on a vitamin E deficient diet and carried through a first pregnancy, then were fed vitamin E and killed during a second pregnancy, had significantly enlarged suprarenals due entirely to cortical hypertrophy. The medulla returned to a normal weight. A fat-free diet produced in male and female albino rats a relative atrophy of the suprarenals due to both cortical and medullary decrease. Curing the symptoms of this diet by feeding fatty acids, chiefly linoleic, did not cause a return of the suprarenal weight to normal. The nature of these relationships is as yet not elucidated.

Dwight L. Wilbur, Rochester, Minnesota.

C. F. SCHLOTTHAUER, V.D.M., AND J. L. BOLLMAN, M.D.

Experimental Gout in Turkeys. Proceedings of the Staff Meeting of the Mayo Clinic, Division of Experimental Medicine, September 19, 1934; pages 560-1.

Gout apparently is a disease of man, birds and reptiles. No definitely proved cases of gout have been observed in lower animals other than the two named. Both visceral and articular gout occur spontaneously in birds; the former is thought to be the more prevalent. Among domesticated fowl gout occurs more frequently in chickens than in waterfowl, and rarely is it seen in pigeons. Gout has been observed in birds of prey in zoological gardens.

During 1933 we had the opportunity to observe spontaneous tophaceous gout in five flocks of turkeys. Since turkeys apparently are susceptible to this disease, and are an easy bird to work with, we attempted to produce gout in them experimentally, for study. We used twenty turkeys in our experiments. They were placed two each, in ten pens. Five of these pens were small cages, measuring 26 by 26 inches (65.96 cm.), within a building, and the remaining five pens were outside runs affording ample exercise and a wide range of temperature. Five combinations of diet were fed to these turkeys. The turkeys in outside and inside pens were fed identically. This gave us the opportunity to study the effects of diet, the effects of restricted exercise, and a combination of the two. The turkeys were fed the following five diets: (1) commercially prepared turkey food containing 20 to 24 per cent protein, (2) commercially prepared turkey food and ground raw horse flesh in equal quantities, (3) commercially prepared turkey food with 5 per cent urea added; (4) commercially prepared turkey food and fresh green spinach, and (5) commercially prepared turkey food and cracker meal in equal quantities.

All turkeys were weighed at approximately the same hour once each week. At this time we also procured 1 c.c. of blood from the wing vein of each, for determinations of blood uric acid.

Little difference occurred which could be attributed to restriction of exercise, except that the restricted animals took less food. This was probably due to the fact that the cages were in a building which reduced the hours of daylight, so that these birds remained on the roost longer than their outdoor neighbors; consequently the value for uric acid in the blood of the restricted birds usually was found to be slightly, but not significantly, lower than that in the blood of the outdoor birds. The birds which were on the standard diet showed a range of blood uric acid, from time to time, of between 4 and 10 mg. per cent, and the birds which received the same diet, with green leaves added, showed a similar range. The diet with meat added gave high values for blood uric acid, from 5 to 22 mg., and the diet with urea added gave similar changes, from 5 to 20 mg. The addition of cracker meal somewhat reduced the level of uric acid in the blood, from 3 to 5 mg.

Part of the uric acid metabolism of birds is like that of mammals, in that uric acid is an end product of purine metabolism, which in turn is part of nuclear metabolism. The major portion of the uric acid formed and excreted by birds, however, is derived from protein or nitrogenous metabolism. These animals possess capabilities for a special process by which urea or ammonia is converted to uric acid by the liver and is excreted by the kidneys as uric acid. Little urea is found in the urine, and the concentration of urea in the blood is low. There are daily variations in the amount of uric acid in the blood, similar to the variations found in the blood urea of mammals. After feeding, the concentration of blood uric acid increases, depending on the amount of protein or nitrogenous substances in the diet, and as assimilation is completed, the value for blood uric acid slowly falls to a fasting level. The bird with free access to food usually eats at frequent intervals, so that the value for blood uric acid almost always is at digestion levels.

Definite gouty tophi appeared on the feet of only those birds in the blood of which the value for uric acid was 15 mg. per cent for at least two weeks. As far as we could determine, the elevated concentration of uric acid of the blood preceded the deposition of tophi and the appearance of symptoms. After symptoms were present, the value for uric acid in the blood usually fell, because less food was consumed. Some of the lesions progressed, to become extremely large and numerous, whereas others developed and remained stationary, but no regression in size or number of lesions was observed.

On the basis of these observations, we feel that tophaceous gout in turkeys depends on marked increase in concentration of uric acid in the blood. The value for blood uric acid may be increased by an increased concentration of nitrogen (either protein or urea) of the diet, or by renal insufficiency.

Frank Smithies, Chicago.

SECTION IV—*Roentgenology*

Roentgenographic Differentiation Between Diverticulitis and Cancer of the Sigmoid*

By

WILLIAM H. STEWART, M.D.

and

H. EARL ILLICK, M.D.

NEW YORK CITY, NEW YORK

WHEN a patient is referred to the roentgenologist for an examination of the colon on account of the possibility of malignancy's being present, one must obtain a very careful history of the case because in the differential diagnosis of the affection this is of vital importance.

Cancer of the sigmoid usually attacks a patient of advanced years, although it may occur at any age. The history is one of a *progressive* lesion without remission and usually of short duration. The patient may have had no symptoms until obstruction occurred, the first indication being in-

*From the Department of Roentgenology, the Lenox Hill Hospital. Submitted October 24, 1934.

Fig. 1. E. M., 42 years. Attacks of sharp shooting pain in L. abdomen for last six days. Constipated. Similar attack one and one-half years ago. Palpable mass in L. L. Q. X-ray findings: Early diverticulitis and sigmoiditis. Mass disappeared under medical treatment.



Fig. 2. M. R., 51 years. For last two years has had a "pulling" sensation in L. side which was painful. More severe in last two months. Mass felt by patient. X-ray findings: Diverticulitis and sigmoiditis. Subsided under medical treatment.





Fig. 3. I. L., 53 years. Attacks of pain and a palpable mass in L. L. Q. Some temperature. X-ray findings: Early manifestations of diverticulitis and sigmoiditis. Subsided under medical treatment.



Fig. 4. I. L. Same as Fig. 3. Ten years later. During this interval patient has been having attacks of pain in L. L. Q. with fever. Palpable mass. Repeated examinations reveal diverticulitis and sigmoiditis. Medical treatment seemed to control attacks. One year later patient died following perforation.

creasing constipation with expulsive type of stools. The frequency of bloody stools with mucus is noticeable in cancer, although frank rectal hemorrhage is not rare. Some cases may have slight pain, although it is more often that pain hardly is sufficient for the patient to consider it serious enough to consult a physician. There is no fever and the blood count may not be affected.

There is often a palpable tumor which never completely disappears; at times it may diminish in size as the accompanying inflammatory reaction subsides. There is only occasionally a rupture into the peri-sigmoidal structures; it causes an "acute abdomen" only when producing intestinal obstruction, which may be sudden. There seldom are any special bladder symptoms in the clinical picture. In malignancy a progressive loss of weight is almost uniformly noted.

In contradistinction to cancer, a patient affected with diverticulitis has a history of recurring attacks over a period of years. The age is most commonly over forty and the lesion nearly always is found in obese adults. A palpable tumor may appear but usually completely disappears unless it is of the dissecting type; then there will remain some induration during the remissions. There are pain, fever and blood count indicating an acute lesion. Cases of diverticulitis often appear as "acute abdomens" and attended with considerable shock. This we note whether there is colon rupture or not. There is always a variable amount of spasm and congestion present in all inflammatory lesions of the sigmoid. We seldom find hemorrhage, although occasionally blood streaked mucus may occur. Recurring constipation is common but there is no characteristic expulsive type of stool. The bladder is more frequently involved with irritative symptoms than is noted in malignancy.

Procto-sigmoidoscopic examination should always be made *before* the cases reach the hands of the roentgenologist for after roentgen examination barium particles often interfere with the clear vision necessary to the recognition of pathology of the colon. In many cases this part of the examination is a failure on account of colon redundancy; in such circumstances, the proctologist is unable to reach the area involved. *As a rule* the endoscopic findings are of great value in the final determination of the diagnosis.

Having obtained a clear history of the case one proceeds with the roentgen examination.

Apparatus: It is necessary to have an apparatus which is capable of switching from fluoroscopic to radiographic control instantly, as during fluoroscopy one often observes something

which it is necessary to record on a film. These reproductions are not satisfactory unless obtained with a more powerful current than is ordinarily used in fluoroscopy, hence the necessity of the "switch over".

Preparation: The colon must be completely empty before giving the barium clysma. This is usually accomplished by giving two ounces of castor oil on the night before the examination, followed by a generous cleansing enema in the morning, to be repeated until the return flow is clear. This cleansing enema is best given an hour before the X-ray examination is to be made. The patient is better able to retain the barium clysma injected in the fluoroscopic room if his bowel has just been emptied.

With a light breakfast allowed, the patient reports to the roentgenologist at about 11 A. M.

Procedure: After having made a *preliminary film* and after proper preparation of the examiner's eyes, the patient is placed on a fluoroscopic table and the *method of procedure* explained to him in order to gain his confidence. The success or failure of the examination may depend upon complete relaxation and respiratory control. In making observations of the sigmoid one meets the following difficulties:

The lower colon usually is freely movable, redundant and curled upon itself. It is situated deeply and surrounded by the pelvic walls and is always difficult to palpate. We eliminate these troubles as much as possible by giving at first only about *one pint* of the barium clysma. This is watched under the fluoroscope with the patient in varying right post-oblique positions. At the most favorable angle the sigmoid is elongated and cleared of overlapping shadows from redundancy of the bowel. It is really remarkable how clearly the entire lower colon then is shown. As only a pint of the clysma is given, this amount is not sufficient to fill the caecum and cause overlying shadows from this part of the proximal colon.

After the rectum and sigmoid carefully have been examined the colon is filled to its complete capacity and then further observations made. The entire procedure is repeated after the patient has *partially* emptied the colon, and again after *complete defecation.*

Often it is advantageous to have the patient return twenty-four hours after passing the clysma. Particles of barium will sometimes work their way into the diverticula and record their presence at this time when the study immediately after defecation has been negative. In the case of the differential diagnosis in complete block of the sigmoid, this procedure is of inestimable

Fig. 5. H. R., 87 years. Constipation. Blood in stools a few times, last noticed two weeks ago. Palpable mass in L. L. Q. Also has hernia in left inguinal region. X-ray findings: Loop of colon in hernial sac. Diverticulitis. No operation. Subsided under medical treatment.



Fig. 6. P. C., 57 years. Pain in abdomen past six months. Lost 35 pounds. Constipated. Palpable mass in L. L. Q. X-ray findings: Large cancer of sigmoid. Oper. findings: Adenocarcinoma of the sigmoid.





Fig. 7. M. J., 48 years. Pain in L. L. Q. for three months. Two months ago had sudden cramp-like pain in L. L. Q., which lasted two weeks. Constipated. Occasional blood streaked stools. Palpable mass in L. L. Q. X-ray findings: Typical medullary carcinoma of the pelvic colon. Oper. findings: Carcinoma of sigmoid.

value. From the procedure as outlined one may judge the amount of time and attention which is required to make a complete and correct X-ray examination. Always we have maintained that should the roentgenologist devote as much attention to the colon as he has been giving the stomach and the gall bladder he would not have to "rush to cover" so often after his mistakes in the X-ray diagnosis of lesions of the rectum and sigmoid have been demonstrated operatively.



Fig. 8. I. K., 66 years. Vague abdominal pains about a year ago, eventually localizing in L. L. Q. Constipated. Loss of weight and strength. Indefinite mass in L. L. Q. X-ray findings: Questionable growth in sigmoid, probably carcinoma. Oper. findings: Scirrhus adenocarcinoma.

Even after exhibiting all this advanced technique one has accomplished but one step in the diagnosis. The fluoroscopic findings must be correlated with the interpretation of the films. It is here that one requires time and patient study before a diagnosis can be made. It is the finer shadows which will tell the story; this is especially so in differential diagnosis. The detection of one or two small sacules at or near the site of the lesion often is a clue which will decide whether

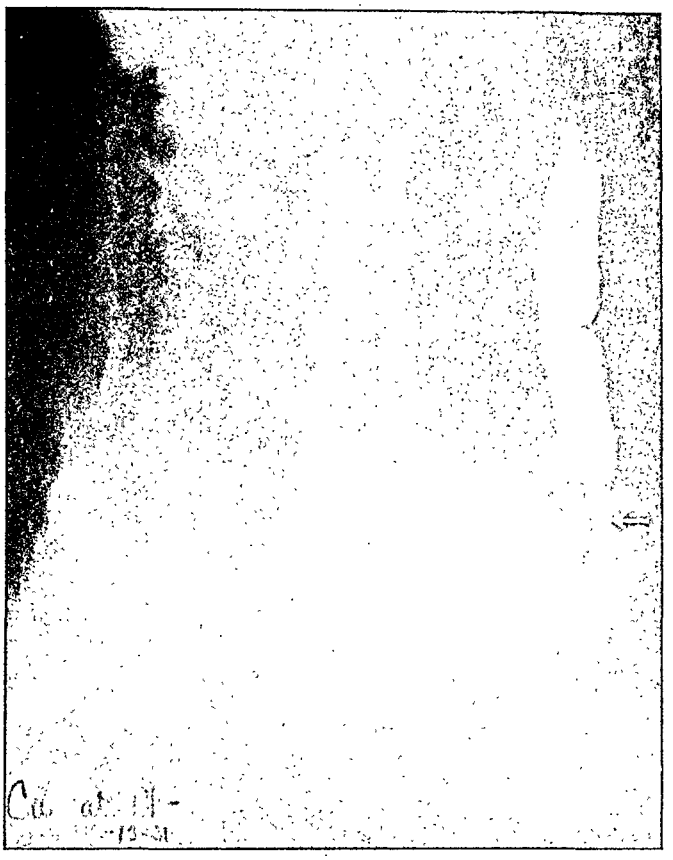


Fig. 9. E. P., 47 years. Constipated. Pain and gas for years. Nine days ago had severe cramp-like pain which lasted 82 hours. Vomiting. Similar attack one year ago. Mass in L. L. Q. X-ray findings: Napkin ring deformity in lower descending colon. Oper. findings: Carcinoma.

one is or is not dealing with cancer. *Our aim is to magnify the image so that all the finer shadows are brought out.* This makes the correct diagnosis much easier and, objectively, more definite.

In some cases, no matter how much care is used, there will be a redoubling of the shadows and the lesion will be covered over. In one patient we were able to demonstrate the cancer by filling only the urinary bladder with water after the colon had been distended with the barium clysma. The raising of the sigmoid by the distended bladder brought the lesion into view.

Fisher's method of insufflating the colon with air after the barium has been defecated is a valuable adjunct. Its special value is in polypoid degeneration of the mucous membrane of the colon or any growth which invades the lumen of the gut rather than infiltrates the walls.

Roentgen differentiation between cancer and diverticulitis of the sigmoid also depends in a great measure upon the type and stage growth of the lesion.

Cancer of the sigmoid has certain roentgen characteristics which must be present before a diagnosis of malignancy is possible. If these are not found, one must be guarded in his statements. Cancerous lesions nearly all show a tendency to canalization. In addition, the mucosal pattern and the haustral markings are destroyed; they are replaced by lobulated, cauliflower masses causing irregular, ragged lumens and finger-print deformity (Figure 7) or they produce a "napkin-ring" defect, with sharp sudden demarcation between normal and pathological involvement (Figure 9). The defects are persistent and usually confined to the lumen of the gut. There is no evidence of diverticula; the mass is "frozen" and exhibits rigidity and fixation. The sigmoid is liable to maintain its patency through canalization and anchorage. The proximal colon is dilated. Sudden obstruction may occur.

Diverticulitis, early, shows a filling defect which results in a serrated or "picket fence" appearance to the sigmoid (Figure 2). This gradually advances until *massive* destruction is in evidence but the mucosal pattern and the haustral markings are seldom completely destroyed (Figures 3 and 4). There is never a crater formation or a napkin ring deformity. The demarcation between the normal and the pathological *is gradual.* There is no incisural contraction. Budding defects can be seen outside the lumen of the intestine, these representing the outward extension of diverticula. These defects, unless the lesion is far advanced, are liable to change in character; at least a portion of the involved colon is flexible. In many instances, the lesion is extra-lumenal, being in the wall of the intestine or in the perisigmoidal structures. Masses of barium may be seen outside the outline of the colon, an indication that diverticula have ruptured. Intestinal obstruction from inflammatory swelling and oedema may occur.

These differential points between cancer and diverticulitis of the sigmoid which have been mentioned are exhibited by the typical cases. Always one must bear in mind that about 2 per cent of cases of diverticulitis undergo malignant "degeneration"; here the signs are rather uncertain. However, when there is a progressiveness to visceral destruction with no remission, combined with a steady down-hill clinical course, invariably such means cancer.

ABSTRACTS

CARTY, JOHN R.; WEINTRAUB, SYDNEY, AND FELTER, ROBERT K.

An X-ray Study of the Post-Operative Stomach. Radiology, 22:191-196, 1934.

A careful clinical and roentgen study was made of 144 cases of peptic ulcer which had been treated surgically. The cases with satisfactory results all showed the stomach much smaller, placed higher and more laterally, with reduced peristaltic activity, lessened mobility, and a much more rapid emptying time. Rapid emptying of the stomach is deemed desirable and in none of the cases did untoward symptoms, such as diarrhea, result. In line with this, posterior gastroenterostomies with large openings placed near the pylorus were most consistently satisfactory.

Poor clinical results were noted in cases in which there had not been a considerable diminution in the size of the stomach, poor drainage being due to one or more of the following causes: the stoma was too small, the stoma was poorly placed, the proximal loop of the anastomosis was too long, the distal loop was kinked at the mesocolon. Emphasis is placed upon making a liberally large opening when operating upon a dilated, obstructed stomach to avoid shrinkage in the stoma as the stomach returns to normal size. A long proximal loop is apt to hinder drainage and establish a vicious cycle. In cases in which severe hemorrhage occurred a considerable time after operation, there being no signs of a recurrent ulcer, the authors found that either the stoma was too small or that the distal loop was obstructed, and offer as explanation the formation of varices at the stoma.

Roentgenologically, poor results are divided into: 1. Those with a disturbance of the mechanical factors, overly large stomach, poor emptying, hyperperistalsis, and poor placement of the stoma. 2. The cases which developed marginal ulcers, formed new ulcers elsewhere, reactivated the original ulcers or developed gastric hemorrhages. Although not relating as causal necessarily, poor mechanical function often was noted in this second group. The authors note a peculiar spasm of the proximal loop in marginal ulcers, and raise the question of its diagnostic significance.

X-ray examination of the post-operative stomach is a vital part of the follow-up study, as there is a definite correlation between the roentgenographic findings and the clinical results, which should lead to a fairly accurate prognostication, from the roentgen study, of good or poor clinical results. Systematic co-operation with the surgeon in this type of analysis should improve the results from gastric surgery by its more satisfactory elucidation of the physiology of the stomach which has been subjected to operation.

James T. Case (Chicago, Ill.).

SECTION VIII—*Editorial*

The editorial contributions published in this Journal represent only the opinions of their writers. Such being the case, this Journal or the American Association is in no way responsible for editorial expressions.

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

ELECTRO-CHEMICAL PROCESSES UNDERLYING GASTRIC AND PANCREATIC SECRETION

FOR years I have been wishing that more experimenters with an intimate knowledge of modern electro-chemistry would interest themselves in the problem of explaining the secretion of HCl by the parietal cells. To me it has always been an astounding fact that these highly specialized cells can secrete hydrogen ions in a concentration a million times greater than that in the blood. One of the first steps toward a solution of this problem was taken when Hollander (1934) showed that the secretion of the parietal cells is nothing more than pure hydrochloric acid in water.

Another splendid piece of work has just come from the hands of Ingraham and Visscher of the University of Illinois. It will appear soon in the Journal of General Physiology. They have obtained a good idea of the electric charge on the limiting membranes of the parietal cells of the stomach and of the alkali producing cells of the pancreas by noting the ability of these membranes to hold back or pass on sixty dyestuffs (injected intravenously), some basic, some acid, and some amphoteric. An important point is that Ingraham and Visscher did not accept the manufacturer's opinion in regard to the electric charge on the color carrying ion in these dyes but checked it by observing the direction of migration in the electric field. In some cases, they also had to study the behavior of the reduction products of these dyes.

The outstanding conclusion arrived at is that all of the dyes secreted by the stomach belong in the basic group except fuchsin S. It is believed that this substance, which did not follow the rule and which was secreted in very small amounts, may have gone through with the mucoid fraction of the gastric juice. Two of the dyes which came through were amphoteric. It should be noted also that fuchsin S is amphoteric when in the reduced state.

All but four of the dyes secreted by the pancreas fall into the acid group and in these four, the chromogen can behave either as a cation or an anion. No typically basic dye was excreted in the pancreatic juice.

A good many of the dyes, when injected intravenously, did not appear in either the gastric or in the pancreatic juice. The reasons for this have not yet been worked out. Theoretically, amphoteric dyes might appear in both the gastric and the pancreatic juices, and this actually happens. Similarly, when the chromogen possesses the property of changing its charge on reduction, it can appear in both juices.

Preliminary studies indicate that the gastric glands have a greater tendency to reduce dyes than have the pancreatic cells. Thus, some of the dyes appeared in the gastric juice in the reduced form, while none of them appeared this way in the pancreatic juice.

It appears from these studies that of all the many peculiarities which characterize the different dyes, the only one which determines their ability to pass through the gastric or the pancreatic mucosa is the nature of the electric charge.

As Ingraham and Visscher point out, the investigator must try to explain not only the foetors which keep one dye from leaving the cell but also those factors which cause another dye to pass through. The writers brought forth considerable evidence to show that the inability of the electronegative dye ions to pass through an electropositive structure is due to strong polar adsorption. They showed experimentally that a collodion membrane impregnated with benzoic acid would stop the passage of basic dyes and let the acid ones pass through. From this and other considerations, they concluded that the membranes across which secretion occurs in the gastric glands must be electro-positive while those in the pancreas must be electro-negative.

The authors discuss at length some of the theories which would explain the passage of some of the dyestuffs through the membrane but much of this is unintelligible to the average physician who is not well trained in physical chemistry, and I shall not try to abstract it.

There are good reasons for believing now that a membrane with properties such as have been demonstrated on the gastric side of the parietal cells should permit the passage of chloride ions while at the same time restraining the passage of the inorganic cations such as sodium. This would account for the passage of the Cl ions toward the lumen of the stomach. The next problem is to explain the passage of the hydrogen ions. According to the theory of Ingraham and Visscher, carbon dioxide can be made to combine with water on one side of a membrane impermeable to cations; the hydrogen ions resulting from dissociation remain, while the bicarbonate ions go through the membrane to balance the influx of

chloride from the fluid on the opposite side. It has been shown by many workers that the amount of bicarbonate in the blood has a decided influence on the secretion of gastric juice.

In a letter, Dr. Visscher writes that, working with Mr. Deutsch, he exposed a Pavlov pouch to roentgen-rays until the gastric juice secreted was alkaline, and he found then that only acid dyes would go through. This observation tends to support the theory of Visscher and Ingraham.

Ingraham and Visscher plan soon to publish a most interesting series of experiments in which they were able to produce HCl with a pH of 2.2 within a collodion sac, the wall of which was impregnated with basic dyes which made it impermeable to cations. The acid was produced by passing a current through suitable bridges, so that the interior of the sac was positive to the exterior. At the same time the material in the interior was kept saturated with CO_2. They believe that in this way they allowed an anion exchange, and permitted the bicarbonate ion to pass back when the chloride ion entered the sac through the cation-impermeable membrane. A similar production of acid was observed when the materials were allowed simply to diffuse, but the process was much slower.

Walter C. Alvarez, Rochester, Minnesota.

NOTICE

The demand for back numbers of this journal has been so unexpectedly large that the publisher is left with only enough on hand to fill orders for bound volumes. To those subscribing to the Journal, it will be encouraging to learn that the publishers are considering planographing all previous issues into an inexpensive edition, provided sufficient demand continues to be evident.

—Sandfield Publishing Co.

SECTION IX—*Book Reviews*

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

This Journal is not responsible for the opinions, decisions or grouping expressed by reviewers of books or pamphlets. For the guidance of readers, an attempt is made to indicate the relative worth of reviewed material by placing "stars"—★ in connection with the reviews. The greater the number of "stars," the more agreeably and importantly has the book or pamphlet impressed the reviewer.

★★★★ *Die Pathologisch-anatomischen Grundlagen der Chirurgie des Rektumkarzinoms*, von Priv.-Doz. Dr. Heinrich Westhues, Erster Oberarzt der Chirurgischen, Universtats-Klinik, Erlangen, Frankfort, A. M. Pub., Georg Thieme, Leipsig, 1934.

(Pathological Anatomy as a Basis of Surgery in Carcinoma of the Rectum, Priv.-Doz. Dr. Heinrich Westhues.)

THIS book is a detailed study of rectal polyps and their relation to carcinoma. The Author believes it possible to recognize the definitely benign polyps and, with some degree of certainty the relatively malignant and relatively benign types. Among the latter are those which are harmless in their early stages. He states that only neoplastic polyps are related to carcinoma, thus simple hyperplastic polyps, *e. g.*, those common in old people (so-called "senile" polyps) and inflammatory polyps are not so related. He feels that the pathologist sees many cases of harmless polyps which never gave trouble and is thus not much impressed but that the clinician's cases are quite different, inasmuch as they give rise to symptoms and are oftener malignant. Non-neoplastic polyps have confused the subject making it appear unimportant.

Westhues' classification, based on anatomic and histologic grounds, designates three groups: *Group 1* are the purely benign polyps; these generally remain benign throughout their course, some may possibly be capable of malignant changes in their advanced stages. Usually they are solitary and have relatively long, narrow pedicles and usually they reach the size of a cherry or walnut. These polyps are not distinguishable from simple hyperplasias, in the early stages of their growth; the epithelium does not differ from normal mucosal epithelium except in mild variations found in some sections of the polyp, where the nuclei have a more rod-like form, more cytoplasm, the cells are more closely packed and mucus production is diminished. These areas are not located in a particular locality but anywhere in the polyp, epithelial changes are hardly more pronounced than occur in purely inflammatory polyps. There are no transition stages between Groups 1 and 2. Only when the growth is as large as a cherry or larger can one be certain of its neoplastic character for purely inflammatory polyps do not become so large. There is no demonstrable relationship between Group 1 polyps and carcinoma.

In the *Second Group* are those polyps in which a progressively spreading epithelial variation occurs. This, an active cell proliferation, usually is first and most typically seen in the neck and peripheral portions of the polyp. These changes early exhibit neoplastic characteristics: an increase in surface epithelium which forms cup-shaped depressions and epithelial knobs or buds. The nuclei are dark, long, narrow and thickly packed. Typically, the peripheral gland-tracts are long with little anastomosis; the central part and base of the polyp resemble the body or fundus of a gland because of a mesh work of ducts with many anastomoses. The epithelial variations here may be, and often are, nearly as great as at the periphery, and they parallel or closely follow the degree of malignancy. Portions of the epithelium are darker than is the same type of tissue nearby especially in the periphery; this is suggestive of, but not diagnostic for, malignancy. Diagnosis must be made by histologic study of the particular area (cell type, cell arrangement, chromatin content, mitoses, etc.). Especially characteristic of this group is an orderly structure, *i. e.*, the stroma is well developed, the gland-tracts rather regularly arranged, and there is no "crowding out" of the epithelial gland-tract variations. Most of these polyps grow to a good size without malignant changes. The extremely large polyps, from walnut to apple size, belong without exception to Group 2. In a large number of cases, polyps in this group become malignant; especially do the large, older growths tend to neoplastic terminations. As to their gross characteristics: the less developed the pedicle the more apt they are to be malignant; conversely, a long, thin, soft pedicle is unlikely to be associated with malignancy. Self-amputation is common to polyps with thin pedicles, hence they do not reach the maturity of those sessile or more firmly anchored by short or broad pedicles.

Group 3 includes polyps with marked epithelial changes; many are carcinomatous. However, there is no basic difference between the polyps of Groups 2 and 3, in fact, the latter are more advanced types of the former. While a Group 2 eventually may become a Group 3 polyp, many polyps originate *per primum* as Group 3 growths. Epithelial changes are more marked in Group 2 than in Group 1, and, in the former, these changes

are characteristically greater in the neck (site of union with pedicle or mucosa) rather than in the body of the polyp. In Group 3, this is even more striking as the actively proliferating epithelium in the neck and, to a less extent in the periphery of the polyp, progresses so rapidly that it overwhelms the ducts and acini of the fundus and body of the polyp and thus these portions often do not have opportunity for complete development. Group 3 polyps, as a rule, have short, often thick, pedicles. The actively proliferating cell mass often forms only a "cap" on a mucosal fold or knob above the mucosal level. Thus there is little pedicle-formation even in the early stage. The process chiefly is epithelial proliferation. This goes on to the development of peripheral gland epithelium down into the neck and body portions, *i. e.*, an infiltration of the relatively less differentiated epithelium into the basal gland zone. However, the process is not so much a spreading growth of epithelium as it is a growth in the depth of the interstitial connective tissue and basal zone. In this way the slower growing, benign mucosa becomes strangulated and disappears. This strangulation of the gland-tract lessens mucus secretion.

In the more malignant of Group 3 polyps, definite carcinoma is seen, at times with carcinomatous invasion through the broken *muscularis mucosae*. The characteristics of this group (3) are: relatively wild epithelial growth, small amount of fibrous stroma, gland tissue destruction, and infiltration. These polyps rarely are larger than a pea and yet many show carcinomatous tendencies.

The carcinomatous polyps of Group 3 are characterized by: irregular structure of the polyp and marked epithelial undifferentiation. Westhues found that definite carcinoma in pea-sized growth was not at all uncommon.

Some pathologists will not fully agree with the Author's deductions or inferences as to the relation of carcinoma to polyps but most observers will credit him with a thorough study of the subject and an excellent presentation of his data.

The book is divided into three sections: First, the general pathology of rectal polyps; second, the growth and local distribution of carcinoma of the rectum as determined by Westhues' own investigations, and third, the clinical application of the study.

In the first section the Author states: "I determined that in about 34 per cent of all rectal carcinomas, their origin from polyps is highly probable. Together with a previously-mentioned 15 per cent of absolutely certain cases, we can state, therefore, that around 60 per cent of all cases (of rectal cancer) can be proved or determined as highly probable to be of polyp origin."

In the second section, Westhues points out that local metastases take place from below upward, that practically they are never below the rectal growth (of course, excluding anal carcinoma). In the last section of his work he states that rectal fixation, in itself, is not a contraindication to operation; that conclusions cannot be drawn from the size of the growth as to either local metastases or those as distant as in the liver.

The Author finds that the demands of complete (radical) resection of the rectum for cancer are fulfilled by excision of the bowel 2 cm. above and below the growth, provided that there is removal of all perirectal connective tissue and fat at its level and 10 to 12 cm. above it. If polyps are present, as often they are, the polyp-bearing area is excised, if it can be safely done. Westhues emphasizes again that most rectal cancers develop from polyps and the majority of polyps become malignant.

This detailed study forms a book of but 112 pages, nevertheless we have reviewed it at length because the work merits description and, we believe, recognition. It is replete with pertinent illustrations of gross specimens, and of microscopic sections. The Author painstakingly has examined a large amount of pathological material; he is a surgeon and writes as a clinician, but his knowledge of the pathology of the affection discussed is impressive. In fact, the major part of the book is devoted to pathology. The subject needs this type of investigation and Westhues' contribution helps to clarify it. The work merits the attention of the pathologist and it will prove a worth-while practical guide to the surgeon.

Clement L. Martin, Chicago.

Academician I. P. Pavlov*

Written in commemoration of his 85th birthday (September 27, 1934) by his former pupil, Professor W. Boldyreff, M.D.,† of Battle Creek, Mich.



An excellent portrait of the world-renowned physiologist, taken in 1926, showing Pavlov just as he had completed an experimental operation.

• IT HAS BEEN my privilege on many occasions to write articles for various scientific journals and societies about my teacher, the famous Russian physiologist, I. P. Pavlov. Those interested will find in these articles his biography and a characterization of him as a scientist, as well as a complete list of his publications.

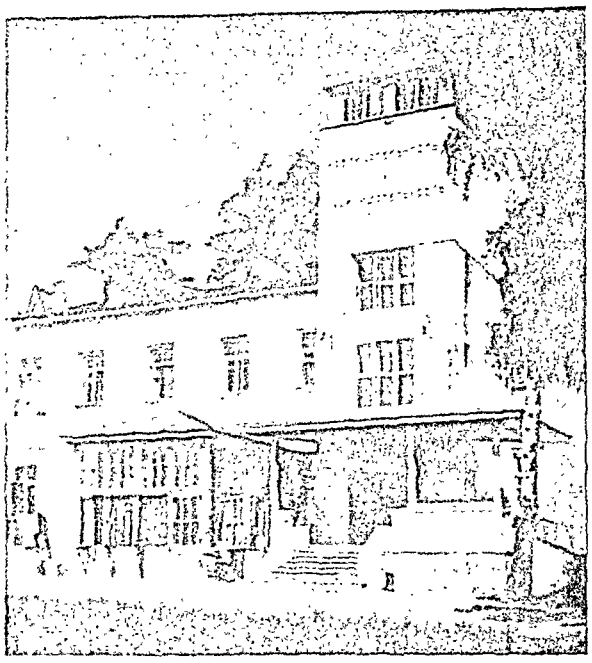
I do not think it necessary here to repeat what I have already written, but I will attempt to sketch briefly the general importance for science and practical medicine of Professor Pavlov's works, and will emphasize those peculiar traits of his personality and manner of work which have particularly helped to further his scientific activities.

There is no question that I. P. Pavlov is not only recognized as the greatest physiologist of our day, but that he stands alone, and beyond comparison with other authorities, in his chosen fields of endeavor, viz., the physiology of digestion and of the significance of reflexes of the cerebrum.

If his work on the physiology of the brain is not yet universally recognized, Pavlov's name in connection with the physiology of digestion is familiar to every student and even to intelligent children in all countries. Therefore there is no need to repeat what everybody knows or go into tiresome details of I. P. Pavlov's work, many of which are difficult for a non-specialist to follow. But it must be stressed that in a large degree his discoveries and other scientific achievements have been accepted into the routine of practical medicine, form the very foundation of the modern teaching on digestion and nutrition and the pathology and treatment of many diseases of the digestive apparatus.

Now a few words about his personality and his manner of work: I. P. Pavlov is not only a famous scientist but also a remarkable man. If it were necessary to define his complex and versatile personality in two or three words, I would say that, apart from his great mind and brilliant

*From The Pavlov Institute, The Battle Creek Sanitarium.
†See also The Bulletin of the Battle Creek Sanitarium for 1923 and 1929, also Izvestia of the Military-Medical Academy for 1904, 1909 and 1914. Abstracts of all works of I. P. Pavlov and his school (up to 1924) may be found in the Archives des Sciences Biologiques, Petersburg, 1904, supplementary volume.
Submitted October 22, 1934.



One of the buildings of Pavlov's new laboratory at Koltooshy, near Leningrad, Autumn, 1934.

talents as a scientist, he is the most diligent, the most indefatigable and the most successful man I have ever met.

Is it not remarkable that at the age of 85 he is not only continuing his scientific work but also performing successful operations on animals for scientific purposes as he has always done? Besides the usual routine in several large laboratories under his supervision, he spends some time of each day in the collection and testing of gastric juice which he introduced into clinical practice as an important medicinal agent in the therapy of certain diseases of the digestive tract.

I. P. Pavlov is not only fond of work but also indefatigable. Having known him for many years (I first met him some 40 years ago), I have never heard him say: "I am tired, I must rest." Not that he wanted to conceal his fatigue, but he knew none. Being a man of rather expansive nature, he always gladly shared with his fellows all his sensations. Also he likes to complain about various real or imaginary unpleasantnesses and inconveniences. But he has never complained of fatigue, seemingly such a feeling being quite foreign to his extremely strong and active nature. This is true both of his physical and spiritual make-up. Strange to say, we, his pupils, a quarter of a century younger than he, often grew tired on various occasions, both in body and in spirit, while he, under the same conditions and working together with us, never complained of or appeared to experience fatigue.

Being a sportsman in spirit and practicing sport all his life, he still wins a Russian outdoor game, "gorodki," which is his favorite pastime. Some thirty years ago, he was one of the best gymnasts in the society of physician-gymnasts which he organized at St. Petersburg. We were all dumbfounded to see him surpass us, still young men, in jumping, trapeze exercises and other gymnastic performances. Only the late Dr. Yawein could keep up to Pavlov's record. Being in excellent health and extremely punctual in all his affairs, Pavlov loved to boast that since the organization of this society (over twenty years before) he had not missed a single meeting. The meetings occurred one evening each week throughout the school year.

Another characteristic trait of Pavlov's is his care to do everything to the best of his ability. Whether he was busy at a scientific investigation of the utmost importance or doing some ordinary, even menial, task, he would always do it with surprising care. "I do not understand," often we heard him say, "how some people can afford to neglect their business. Even if it were the smallest thing, for instance, sweeping the floor, carrying of loads, etc., one must apply to it all his energy, all his attention, in order to do it in the best way. This would be the most cheerful, the most pleasant and the most profitable way." And Pavlov practices this rule himself in all his actions.

Now it is quite natural that with his richly gifted nature Pavlov has achieved such brilliant success in science and occupies the high position that he does today. It could not be otherwise.

There are two other factors which are in his favor: he is extremely lucky and exceptionally healthy and strong. Pavlov's success was owing to some traits of his character as well as to the fact that he always had favorable conditions. Some people are extremely unlucky, failing in everything, while others are "born under a lucky star." Pavlov is a typical example of the latter. Luck has followed him everywhere. Even the Bolsheviks have made an exception for him alone among all Russian scientists and arranged for him better conditions of life and work. He was also a favorite of the Czar's government.

One must not pass in silence Pavlov's rare and unswerving moderation which he practices in all things, except work. It is surprising that in him moderation is reconciled with an indomitable, passionate nature and excessive enthusiasm. Doubtless his moderation has helped him to preserve his health and vigor into old age. Not so long ago he told us: "I always rise from the table before I am quite satisfied, while I still have a desire for another bite of something. Thanks to this rule, I have preserved my stomach in perfect order." He has seldom been sick and when he is, he does not go to bed, nor does he stop working. He quits eating. Complete fasting for a day or two is of great help to him in disease.

A few words about the main scientific idea, or rather the main rule of Pavlov, during all his long and fruitful scientific activity. While still

I. P. Pavlov's latest portrait. Autumn, 1934.



a young man, working with the problem of blood pressure, he decided that the universally accepted method of vivisection does not bring real results. For, during a vivisection the animal is tied up, suffering, and crippled or poisoned by various substances which would make him less resistant to the experiment, and losing much blood.*

Pavlov always succeeded in anything that interested him. He began doing small operations on the dogs the night before their blood pressure was to be tested, introducing into their blood vessels, and fastening, the tip of the apparatus used for measuring the pressure (a glass tube, or cannula). All this was done with the utmost care not to contaminate the wound with microbes and to give the animal the least possible pain. The wound was then sutured and closed. Next day the dog did not differ from any other healthy dog in his appearance or behavior. Quite painlessly, and often unnoticeably, connecting the cannula with the mercury manometer, Pavlov first obtained the true figures for blood pressure in the vessels.

In the execution of such minute experiments which even now no one but he can perform, Pavlov was assisted by two factors (1) his extreme adroitness and his experience,† and (2) his knack of securing the affection of the animals,†† which he always loved and pitied and which in return readily obeyed him. However, when the work required it, Pavlov did not hesitate to subject his animals to vivisection and operations which would cripple them for life, but he always avoided causing unnecessary pain.

When later Pavlov began working in a quite different field—the physiology of digestion—he applied and practiced his main principle, which is to conduct experiments and obtain all data in perfectly normal conditions of the experimental animal. For this he made beforehand some preparatory operations so that the organ that was the subject of study would be easily accessible without causing any pain or discomfort to the animal. He has almost abandoned vivisection in his scientific research, replacing it by his new humane and highly fruitful method.

When it is necessary to study the secretion of the gastric juice, a small separate pouch is cut out from the dog's stomach, under anaesthesia and with all the regulations employed in operating on human beings. Food does not reach this pouch, but during digestion some pure gastric juice gathers there, being secreted by the gastric mucosa, as sweat is secreted by the skin. This pouch has an opening outside in the dog's abdomen (these operations are usually made on dogs). The animal loses a small amount of gastric juice, without any injury to his health, and furnishes the investigator with a nearly complete and exact picture of what goes on in the real stomach during the digestion of food. Thus originated the famous Pavlov's "isolated pouch." Not until one or two months after the operation, when all is healed and the dog has quite recovered, does Pavlov begin to stage his experiments.

*At present, and perhaps in the future, the vivisection method will be indispensable, irreplaceable and very useful. Whole branches of our science are able to continue working only with its aid (for instance, chapters on the peripheral nervous system, on blood and lymph vessels, etc.). Even in the study of digestion, often one cannot avoid vivisections. In the value of data obtained, this method stands much higher than experiments on organs extirpated from the body, although they are also of certain incontestable advantages. Every laboratory method has good and weak points. As for the seeming cruelty of vivisection, this is either an exaggeration or often complete misrepresentation. With a trained worker (or in the ordinary university laboratory), the vivisection method is not any more cruel than any other method. The antivivisection tendency now at work among certain circles of the American society should be considered as a dangerous prejudice. Vivisection is indispensable for the development of medicine. It gives knowledge necessary not only for treatment of human beings but of animals as well. There is no other way to obtain this knowledge. If for some reason vivisections were abandoned, necessary experiments would be made on human beings, sick and healthy, and that would be atrocious, indeed.

†He is ambidextrous, but his left hand is more skillful in all surgical operations. In his young days, before he had assistants, he used to perform alone and sometimes even with one hand complicated tasks (as for instance introduction of a cannula into the salivary duct) which ordinarily require combined efforts of two or three people. Later, I often assisted him during his operations and comparing his surgical technique with that of other Russian and foreign famous surgeons I must admit that Pavlov was not at all inferior to them in adroitness and successful results. The same opinion was held by I. M. Sechenoff on the vivisectional art of Pavlov, as compared with Cl. Bernard. The late Professor R. Tigerstedt (of Helsingfors) once watched one of Pavlov's favorite operations (dissection of the spinal cord under the brain), expecting it to occupy 20 minutes. He could not see the entire operation, as the dissection was to be made deep in the wound. In two minutes after the operation started Tigerstedt asked Pavlov how soon he would begin the dissection. "I have just dissected the spinal cord," was his answer—"the operation is finished."

††In his youth, an ardent scientific worker but unable to afford sufficient means to build a special pen for the dogs that had been operated upon, Pavlov used to keep them in his own room until they recovered. According to him, this forced and extremely inconvenient company was of great service to him then and in his future scientific work, giving him a chance to note some important details which would otherwise have escaped his attention.

If he wants to study gastric movements, he makes a window in the stomach, or a fistula, opening directly outside and when necessary closed with a cork stopper like a bottle.*

Pavlov treated the whole digestive apparatus in the same manner, not the stomach alone, and he proved to be a great master in inventing suitable operations and laboratory environment for the better application of the same.

For his operations, Pavlov built a special surgical department in his laboratory (at the Institute of Experimental Medicine in 1891), where each dog subjected to operation has a separate compartment kept ideally clean and under permanent care of trained servants. In reality, such dogs often receive better care than some patients in hospitals and clinics. The same opinion has been expressed in print by Dr. John Harvey Kellogg, who knows Pavlov's laboratory well and who has for over sixty years collaborated with various clinics and hospitals of Europe and America.

It is natural, then, that the animals upon which he has operated love Pavlov and readily approach him during experiments. Animals have well rewarded him, assisting him to be the first to obtain correct and complete knowledge regarding most aspects of digestion. In other words, Pavlov has succeeded in making the physiology of digestion an exact science, or as he says himself, in putting it "on the right track."

But now he decides to subject to the same exact and many-sided analysis the most complex and the most enigmatic side of the living being—his psychical activity. He was clever enough to apply, in this mysterious realm, and put to successful use the same basic principle which proved to be so fruitful in his other scientific work.

This transition from the studies on digestion to the realm of psychology was not accidental; it was not a fancy of the scientist or an adventure. Neither was it a jump into the unknown over a precipice, but it was a natural and gradual development.

Studying the phenomena of the digestion of healthy animals, Pavlov had constantly to face psychical influences which sometimes greatly assisted the digestive processes, and sometimes acted as powerful inhibitors. In this manner Pavlov and his pupils gathered a vast material of a purely psychical nature, gleaned in the field of the physiology of digestion. They noticed, for example, that the very sound of the footsteps of the servant who feeds the dog causes an abundant gastric and salivary secretion in the dog. They found it possible to study in detail and with exactitude the phenomena of memory, building from similar data regarding salivary secretion, and so forth. Other important observations in the realm of the psychic life of the animal have been gathered as a by-product of the experiments with digestion.

The value of this rich material consisted mostly in the fact that one could study psychical phenomena in animals from their physiological angles, using the method of Pavlov. Psychical processes are accompanied by corresponding physiological phenomena, such as the secretion of saliva or gastric juice. Measuring the quantity and checking up on the chemical properties of these juices, Pavlov learned to draw correct conclusions as to the animals' psychical states, which were altogether inaccessible to the former well-known methods of psychologists. Psychical phenomena are complex, fleeting, elusive and mysterious, while their physiological reflections or counterparts are comparatively simple, tangible, easily reproduced and may even be measured.

Having transferred his attention and work to the psychic realm of animals, Pavlov decided to do the work in a strictly objective manner, according to his own plan. This was purely physiological. He completely avoided the use of psychological terms and data gathered formerly and still in use by psychologists and psychiatrists. He introduced his own method, an original one, exact and dependable, based on the work of the salivary gland, salivary secretion, more or less connected with the psychical state of the animal. This method is based on the study of psychic reflexes (or all vital phenomena produced by outside causes and regulated by the brain), which Pavlov called "conditioned" as contrasted with "unconditioned" or physiological reflexes.

Saliva is secreted not only during eating (physiological or "unconditioned" reflex), but at the very sight of food, or even when only its odor or some noise connected with it are apparent (psychical or "conditioned" reflex). Thoughts of food may also cause a secretion of saliva. It may also occur at the sight or at the mere recollection of something nauseating. All these are conditioned salivary reflexes, which are also called natural as distinguished from the artificial.

Pavlov's school seldom uses natural conditioned reflexes for scientific observations. These reflexes are for the most part inborn, and always old and therefore with the course of time they are combined with other psychic influences. For that reason they often present a complex picture, too cumbersome for the investigator. Simple artificially created reflexes are much more convenient and dependable for his purpose.

Here are some examples of artificial reflexes: If a dog is fed a certain food many times and at the same time is shown a certain object, or hears a certain sound (instead of the organs of sight and hearing one may excite the organs of smell, touch, etc., with equal success), in the course of time, after a series of such combinations, a strong association is formed between the named irrita-

*Such operations do not decrease the vitality of the animals and they live afterwards just as long as they would otherwise. I like to recall that the famous American trapper, Alexis St. Martin, who had a gastric fistula as a result of a serious accidental wound at the age of 19, lived with it until the ripe age of 83, even in spite of the fact that he was an inveterate drunkard into the bargain.

Of course, there are cases when certain diseases are purposely produced in animals that shorten their life; but these are exceptions from the general rule.



I. P. Pavlov with his family, holding a granddaughter in his lap. July 31, 1934. First row, second from left, Mrs. I. P. Pavlov holding another granddaughter; second row, second and fifth from left, are I. P. Pavlov's sons.

tions and the food. Sound or sight of certain things become signals of feeding time for the animal. The mere showing of an object which was used for such experiments, or the hearing of a sound, will cause a secretion of saliva having the same properties that are found in it during the eating of this particular food.

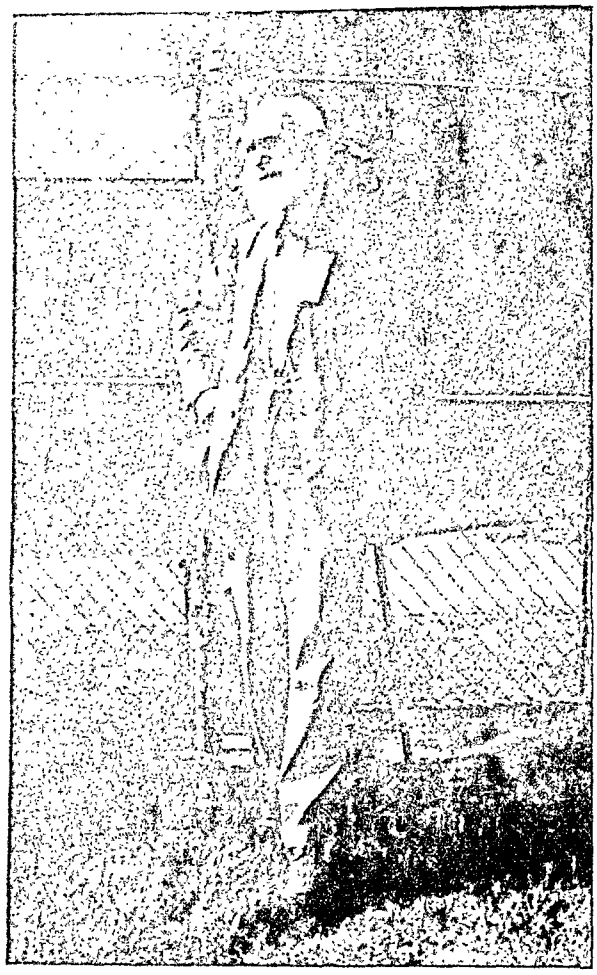
In this way any outside influence which is reflected in the psychical life can be connected with the salivary secretion. And from the salivary secretion one can judge about the psychical state of the animal, or, as Pavlov said once, we can "study a man's soul in his spittle."

A pupil of Pavlov, Professor N. I. Krasnogorsky, proved later that all material gathered by the Pavlov school in the realm of conditioned reflexes in dogs, is also true as applied to human beings.

Following his plan, Pavlov and his school study psychical phenomena by simply keeping a record of the animal's behavior, his reactions to various acts of the investigator; but the most part of the work is based on the measuring of the quantity and properties of the saliva secreted. Quite banished are all thoughts about what the animal may think, feel, wish or fear, as being a loose, uncertain ground on which one should not try to build the new edifice of objective physiology of brain and sense organs.

Independently and almost simultaneously with some American psychologists, styled "behaviorists" (Thorndyke, Watson and others) because they study the outward behavior of animals, Pavlov has arrived at the same plan.

Psychical phenomena are very complex. In animals they occur simultaneously in multitudes, affecting each other in certain ways and thus making their study infinitely more complicated. Besides the influence of the investigator, there are often foreign effects from outside influences which steal their way into the experiment and spoil the whole thing. So, for instance, when a dog is tested for his sound, smell and sight reactions, he may perceive other sounds coming from the street and react to them in a forceful manner. For this reason, Pavlov thought of building isolated experiment rooms, perfectly shut off from the outside world. In the study of digestion a portion of the stomach, now the whole organ was isolated. But dogs possess such fine hearing and sense of smell. Pavlov had to erect a special building at the Institute of Experimental Medicine (in 1910) which cost over 200,000 rubles. In outward appearance it resembles a medieval castle or a prison, in its thick wall, few small windows and a ditch surrounding the entire construction which prevents transmission of sounds through the soil.



I. P. Pavlov in America in 1929.

There are several experiment rooms, each one designed for one dog, and sound-proof for outside noises. The dog is completely isolated. But the investigator may, unwittingly, influence the dog and complicate or spoil the effect of the experiment. Pavlov has removed this seemingly insurmountable obstacle by dividing the room into two partitions with a wall; in one part is the dog, in the other part the man. The experimenter has at hand various complicated apparatuses through which he has contact with the dog and he can watch the dog through a field glass (or periscope) built in the wall. In the perfect arrangement of this experiment room Pavlov's method is superior to that of the behaviorists.

In the equipment of this room Pavlov's oldest assistant, E. A. Ganike, proved to be of inestimable help. Being a past master in theoretical and applied physics and mechanics, and a born inventor, he has built a great number of various clever apparatuses which are exact and noiseless. Some of these devices show or give the animal some food, others introduce simultaneously the desired irritant (sound, light, temperature, etc.), still others record the number of falling drops of saliva, and so forth.

Both in the physiology of digestion and in the domain of conditioned reflexes Pavlov was not satisfied with a study of the normal state of animals alone, but has also studied pathological phenomena. For that reason his works are vitally important and are of value in treatment of diseases of the digestive tract and those of the brain. Both somatic medicine and psychiatry (including many nervous disorders) are about equally indebted to Pavlov.

In the course of all his scientific work repetition of the same experiments played a very important role. According to the Latin proverb, "repetitio est mater studiorum". In this we see another characteristic trait of Pavlov, he is systematic. Although he is of purely Russian origin (most of his ancestors were of the clergy) he is as systematic and accurate as a proverbial German.

Pavlov never spares time nor work when he wants to repeat the same experiments on the same or on a new dog. And he does not find it tiresome or monotonous to go through the same experiment scores, hundreds, thousands of times. Such is his system. Through juxtaposition of a series of similar experiments he can establish their important findings of permanent value and discard whatever is secondary or accidental. Of course, a great deal of material is thus wasted, but whatever is saved for publication is unquestionable and clear. From heaps of sand gathered during months, finally a few grains of pure gold are sifted out.

In the process of collaboration, through intensive work and constant repetition of experiments and their criticism, not only the scientific truth is established, but methods of exact investigation are developed. Pavlov's laboratory holds the first rank in the world and should be a model for all other laboratories. Nothing is done at random, without a strictly definite plan, in his laboratory.

It is utterly ridiculous how some investigators, possessing neither the talent, nor the skill, nor the scientific fervor of Pavlov, in their vain race after cheap fame, declare that they have discovered flaws in Pavlov's statements and errors in his data and attempt to correct these so-called mistakes. Such "revisions" sometimes take us some 50 or more years back in scientific progress.

Such work requires many helpers. Pavlov has a rare gift of attracting and inspiring collaboration. Even plain laboratory servants, half-illiterate peasants, under his enthusiastic and contagious influence often were converted into science workers. Pavlov used to say: "An old, experienced laboratory servant is more useful in the laboratory than a young professional assistant."

At the Institute of Experimental Medicine, there was one such man, Nicolas, an excellent caretaker, who was also very valuable as an ob-

server and animal trainer in laboratory work. Even in experiments he often proved to be a strict and indispensable teacher for beginning physicians, including myself. There was a boy, Vania Shoovaloff, who began working in physiological surgery at the age of fifteen and at twenty-three was an accomplished and experienced surgeon-physiologist. Pavlov was planning to promote him to the rank of his chief assistant surgeon and to obtain for him the necessary scholarship to complete his education. Sudden death from typhoid fever stopped this career. There were other such examples (Mr. Sergius Ignatievich Nikolaeff at the Medical Academy, who was elected a member of the Russian Physiological Society in 1928).

Pavlov's laboratory was always full of collaborators. At present he has fifty assistants. He knows how to keep them all busy and they learn to like their work. Work goes on in a regular routine, in this scientific factory, day and night, if necessary. Its productive power is astounding. But far from all the material is published at once. It must pass the test of severest criticism and control experiments by all members working over the given problem, and by Pavlov himself; only the most essential and strictly confirmed portion then is published. Personally, I used only one-tenth of my experimental data for my dissertation; some of that material was published later separately, but about three-fourths of all my scientific baggage, obtained in Pavlov's laboratory, has never come to light in print.

Pavlov has many imitators and followers in Russia and abroad who copy his laboratory arrangement and his experimental technique. Some work with digestion, others with reflexes. Among such pupils and followers we may name Prof. E. S. London (Petersburg), Prof. A. Bickel (Berlin), Prof. A. J. Carlson and Prof. A. C. Ivy (both of Chicago), Prof. V. M. Behtereff (Petersburg), and many others. The first four of these men are working with problems of digestion. Behtereff, being a psychiatrist, devotes his time to conditioned reflexes, which he calls "combining-motor". When he first started to work in this field, his assistants constantly came to us for references and instructions, which were gladly given; and once (in 1905) Behtereff himself came to our laboratory at the Military Medical Academy and watched everything in detail.

Among clinicians the first men to pay attention to Pavlov's work and to put his teaching to systematic use with great benefit for their patients were, in Russia, Professor A. E. Yarotzky (Moscow) and in America, Dr. J. H. Kellogg (Battle Creek, Michigan). Soon other physiological institutes copied from Pavlov's laboratory, began to grow, at first in Russia, and later in Europe and America. I have had the opportunity to visit scores of them in all parts of the world. Truly, Pavlov has become a universal teacher of experimental physiology. He has not worked in vain: his efforts have borne abundant, fine fruit and are recorded in textbooks of physiology and medicine.

At the recommendation of Dr. V. L. Kellogg (head of the National Research Council in America) and with the offer of Dr. J. H. Kellogg (Director of the Battle Creek Sanitarium), I organized in 1922 the Pavlov Physiological Institute at this Sanitarium, and in the summer of 1923 we had the honor of receiving Pavlov as a visitor. He spent a week with us.

On the American soil we are conducting scientific work in the method of the great Russian physiologist. Since the opening date, this laboratory has issued about one hundred published works, either in scientific journals or as monographs, in America, France, Germany, Italy, Sweden, Switzerland, Japan, Yugoslavia and Russia.*

Pavlov has always been a great admirer of America. He came to this country twice: in 1923, when he lectured in several American Universities, and in 1929 to attend the Thirteenth International Physiological Congress in Boston and the Ninth International Psychological Congress in New Haven. At both these gatherings Pavlov gave reports which were enthusiastically acclaimed by both scientists and the attending general public.

Today, at Koltooshy, near Petrograd, construction is being completed for a second large laboratory for Pavlov for the study of conditioned reflexes. It covers a large piece of ground (several square miles) and cost several million rubles. It will house apartments for Pavlov, other science workers and employees, as well as contain specially constructed, fine compartments for hundreds of animals.

This laboratory of Pavlov, where conditioned reflexes are being studied, has two branches, one in Leningrad, and one at Koltooshy, is now unique in the equipment and personnel, just like Tycho

*LIST OF COLLABORATORS
AT PAVLOV PHYSIOLOGICAL INSTITUTE

Name	Number of Published Works	Published in:
J. H. Kellogg, M.D.	4	AMERICA
C. E. Stewart, M.D.	4	
J. T. Case, M.D.	4	FRANCE
W. F. Martin, M.D.		
A. B. Olsen, M.D.	1	SWEDEN
C. C. Hubly, M.D.		
A. H. Kretchmar, M.D.	1	GERMANY
W. B. Lewis, M.D.	1	
C. E. Roderick, M.D.		ITALY
N. O. Byland, M.D.	In preparation	
A. Humphrey, M.D.		JAPAN
Jean F. Stewart, M.D.	6	
E. Boldyreff	26	YUGOSLAVIA
A. W. Boldyreff	9	
J. W. Boldyreff	2	RUSSIA
Tatiana W. Boldyreff	In preparation	
E. S. Boehm		
Madelyn Williams		
J. Benfeld		
Margaret Granger	1	

Between 1923 and 1934, together with Dr. W. N. B.'s papers, the total number of publications is about 100.

Brahe's Uranienborg in Denmark was in the sixteenth century a unique astronomical observatory.

Upon the occasion of Academician I. P. Pavlov's eighty-fifth birthday, he was granted a life pension of 20,000 rubles a year; five scholarships bearing his name, 6,000 rubles each, will be offered, and a fund of 1,000,000 rubles is being reserved for elaboration of his laboratory experiments.

The Academy of Sciences (Leningrad, Russia) will soon begin a complete edition of this scientist's collected works.

Why is the Soviet government, interfering with free science and mercilessly killing scientists and their families, so favorable toward I. P. Pavlov? One of the reasons for their favorable attitude is easily apparent in reading the following passage from the official monograph dedicated to description of the Institute of Experimental Medicine: "I. P. Pavlov is in charge of the main department of the Institute, the Physiological, which is occupied with the study of highest nervous activity. Outside of its great scientific interest, this problem has a great social importance, since here the scientists possess strictly materialistic data from which they very clearly prove the correctness of materialistic doctrine and discard the scholastic invention of human 'soul'."*

Pavlov does not like to write. He has not published one book, with the exception of his lectures. But his lectures are famous and have brought world-wide glory to Russian science. Of such lectures there are three kinds: (1) Lectures on the physiology of the main digestive glands, read to physicians at the Institute of Experimental Medicine, published in 1897; (2) Physiology in Experiments, lectures to the students of the Imperial Military-Medical Academy (first edition in 1899), and (3) Conditional Reflexes, lectures to the students of the same Academy and other audiences (in 1924). Altogether Pavlov has published over one hundred articles in the principal European languages.

As once D. I. Mendeleff for sciences and L. N. Tolstoy for literature, so now I. P. Pavlov is a flaming torch, a great spiritual power, glorifying the Russian name in his native land and far outside its frontiers.

*N. Egoroff, p. 13, Sources of Sciences. State Institute of Experimental Medicine. Edition of Narkomsdrav, S.R.F.R.S. (U.S.S.R.), year of publication not given—about 1928—printed at Leningrad.

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ACKNOWLEDGMENT

This list has been kindly supplied by Professor I. P. Pavlov's son and secretary, Mr. Vsevolod Ivanovich Pavlov, whom I thank most cordially for the information.

Physicians desiring to contribute to this section, After "Hours," are requested to forward their manuscripts, accompanied, if possible, by illustrations, well in advance of the date desired for publication.—Editors.

SECTION XII—"*The Clinic*"

Polyposis of Duodenum and Jejunum...Report of An Instance

By

JOHN M. CASSIDY, B.S., M.D.*

and

BENJAMIN J. MACCHIA, M.D.
JERSEY CITY, NEW JERSEY

THE rarity of polyposis of the upper third of the small intestines and the possibility of these "new growths" clinically simulating peptic ulcer have led us to report the following case and to review the available literature.

CASE REPORT

J. A., age 29, male, white, was admitted to St. Francis Hospital because of *vomiting*. He had been symptom-free until ten days before entrance when he complained of a "heaviness in his stomach" which soon gave way to periods of vomiting. This act occurred several times a day and was always preceded by nausea. Generally, it came on about three to nine hours after eating and exhibited especial aggravation towards evening but never occurred during sleep. The vomitus had been moderate in amount ranging in color from "black to white" and was occasionally streaked with blood. Frequently the vomitus contained many particles of undigested food.

Pain began soon after the onset of vomiting. It was described as sharp, peri-umbilical in location and as regularly recurring one to three hours after each meal. It always was preceded by a "bloated feeling" about the umbilicus spreading laterally and occasionally radiating to the lumbar spine. It would last one-half to four minutes and was completely relieved by the vomiting and food intake but not by soda. This pain followed the intake of fluid as well as solid foods.

Anorexia was experienced. Solid food had not been retained for the past ten days. Belching was frequent and obstipation troublesome. Stools on several occasions had been "tarry". An occasional fleeting abdominal cramp had also been noted. The patient had lost twenty-seven pounds in weight within the past year.

Except for slight dyspnea on exertion and occasional nocturia with passage of "red urine" the remainder of the history of the present illness was negative.

Family and personal histories were negative.

Past history revealed patient to have had "ptomaine poisoning" at fourteen years of age; recent pyorrhea and gonorrheal infection in 1925; respiratory *la grippe* in 1930.

Examination

Patient was a male, white, adult, about five feet six inches in height, weighing one hundred twelve pounds, and lying comfortably in bed. Belching was constant during the examination. The skin was pallid and dry with a faint blush about the cheeks. *Tache cerebrale* was easily elicited. Eye-grounds revealed early angiosclerotic changes. Slight anemia of the mucous membranes and *fetor ex oris* were noticeable. The tongue was heavily coated and dry; the lips were dry and chapped; the gums were reddened, slightly swollen and blood streaked. Some evidence of peripheral arteriosclerosis was noted. The blood pressure was 126 systolic, 68 diastolic. The heart and lungs were normal.

The abdomen was somewhat scaphoid and slightly rigid throughout. The sigmoid was spastic and moderately tender. The cecum was dilated and contained gas and fluid. On rectal examination the sphincter was normal, the ampulla contained a few small hard fecal masses. Both seminal vesicles were palpable and slightly tender; the prostate was somewhat boggy. A small thrombotic pile was visible externally.

Tentative diagnoses of bleeding duodenal ulcer with pylorospasm, hemorrhagic gingivitis and chronic Neisserian infection were made on admission.

Clinical Course

The patient was immediately given routine ulcer therapy with prompt abatement of all symptoms. The vomiting ceased, the pain disappeared completely and the bowel movements again became normal. There was a gain of 5½ pounds in five days.

However, this improvement was only transient. On the sixth day the original symptoms returned but the pain now was colicky in character and independent of food intake. There was no doubt that now we were dealing with a chronic high intestinal obstruction. There were several such remissions during which bowel stiffenings and peristaltic waves were observed together with constipation, vomiting, tarry stools and increasing anemia. While preparations were being made for transfusion and laparotomy the patient died and a partial autopsy was obtained.

The *temperature* never exceeded 100.4° except just before death when it rose to 103.6°. The *pulse rate* ranged from 70 to 110. The respiratory rate was normal throughout the course. *Edema* of the lower extremities, and bloody urethral discharge were late manifestations.

Laboratory Data

Tuberculin test was negative. Urinalyses were negative except for the presence of a slight trace of albumin on two occasions. The red blood corpuscles dropped from 4,600,000 on admission to 2,400,000 and the hemoglobin from 80 per cent to 45 per cent before death. The white blood corpuscles ranged from 14,750 to 8,500 with normal differential values.

The blood sedimentation time was normal. Blood non-protein nitrogen 46.1 and creatinin 2.3 mgs. per 100 c.c. blood. *The stools were positive for occult blood on seven occasions.*

*Attending Physician, St. Francis Hospital.
Submitted November 12, 1934.

The sputum was negative for tubercle bacilli. Gastric analyses revealed achlorhydria on several occasions with total acidity of 6 and absence of occult blood. Blood Wassermann and Kahn were negative.

Radiologic Data

Roentgenograms of the chest and urologic tract were negative. A gastro-intestinal series revealed *defective duodenal bulb*, cecal and colonic stasis for which a diagnosis was offered of duodenal ulcer with adhesions in region of gall bladder. (Figs. 1 and 2.)

A "scout" roentgenogram revealed a dilated jejunal loop in the left side of the abdomen with two suspicious dense shadows along its lateral border.

Autopsy Report

Gross findings: Intussusception of the jejunum with early gangrenous changes.

There were seventeen polyps located in the first 31 inches of the gut, eight of which were in the duodenum. The polyps had broad bases several of which were ulcerated and ranged in size from a marble to a chicken's egg. The largest was 16 cm. in circumference and was situated directly opposite the papilla of Vater. No metastases were found. (Fig. 3.)

Microscopical report by Dr. Gnassi of the ulcerated polyps returned a diagnosis of adenocarcinoma.

COMMENTS

This case was exceedingly interesting not only because of its rarity but also because of the character of its early course. As is readily seen, the syndrome of peptic ulcer closely was simulated. The tarry stools, the defective duodenal bulb, the hematemesis and the abrupt termination of the symptoms following ulcer therapy strongly supported the primary diagnosis.

However, a complete change in the clinical picture soon was observed. Vomiting, obstipation, melena, with ephemeral remissions, followed with even greater severity. Recurring abdominal colic became a conspicuous symptom. The remissions were no doubt due to the spontaneous reductions of an intussusception. A peculiar phenomenon known as "Steifung" appeared, as evidenced by the tetanic stiffening of more than eighteen inches of the intestinal tract. This enterospasm lasted more than two hours and was not affected by atropine sulphate, grains 1/50, intravenously.

The achlorhydria, with low total acid also was a persistent feature during the course of this disease. We consider this finding as an important differential point between ulcer and high, chronic intestinal obstruction by polyps. It was found in almost all of the cases reported below in which gastric analyses were done.

In Figure 1 is seen the dilated jejunal loop with the two dense masses protruding into the lumen from its lateral wall. These masses, although incorrectly interpreted, were later shown to be due to the jejunal polyps. To our knowledge a similar picture or report of visualization of polypi in the jejunum by means of a "scout" roentgenogram could not be found in the literature. Figure 2 is a six-hour

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film showing a dilated jejunal loop and several ring shadows of barium surrounding the polyps. These ring shadows when present are very characteristic of polyposis.

REVIEW OF LITERATURE CONCERNING POLYPOSIS OF THE DUODENUM AND THE JEJUNUM

The comparative rarity of polyposis of the upper third of the small intestine is attested by a review of the literature. The first case of record was that reported by Cruveilhier in 1834 (Quoted by Golden)[1] where there were two sessile adenomas of the small intestine, the larger one about the size of a walnut. Von Rokitanski was apparently acquainted with high lying polypi for he recognized the fact that intestinal polypi might undergo malignant degeneration. In 1897, Kanthack and Furnival[2] exhibited a necropsy specimen before the Pathologic Society of London in which the jejunum was studded with small polypoid excrescences. Hauser, in 1895, reported a case of polyposis of the entire gut, a walnut-sized ulcerated polyp being present at the junction of the descending and the transverse limbs of the duodenum. Weschselman, in 1910, described a case of polyposis in a man 62 years of age involving the entire gastro-intestinal tract, with the exception of the ileum. Washburn[3] reported a male, aged 21 years, who had gastric upsets for eighteen months and who, at operation, was found to have multiple polypi of the jejunum necessitating resection of five feet of gut. Maunsell[4] mentions two cases which were diagnosed as gastric ulcer in whom at operation sessile tumors of the jejunum were found. In one of these, the roentgenogram revealed duodenal retention. Higgins,[5] in 1931, stated that papillomata are almost unknown in the jejunum and mentions five cases of benign tumors of the jejunum which he was able to find in reviewing literature as far back as 1835. Also he stated that he was unable to find any record of a roentgenogram revealing these tumors. He cites a case diagnosed as pyloric stenosis which, at operation, proved to be a polypoid tumor, four inches from the duodeno-jejunal junction, causing intussusception. The roentgenologic examination revealed an enormously dilated duodenum and slight gastric retention. Wellbrock,[6] in 1831, reported two cases of jejunal neoplasm in one of which achlorhydria was present. Heng-Liu[7] mentions three cases of non-malignant, papillary adenoma in one of which the lesion was found in the jejunum. Recently, Farmer[8] cited a case in which diagnoses of gastric ulcer and gastric neurosis had been made but at operation two jejunal polyps were found and excised. Cases of jejunal polyps also were reported by Somerville-Large,[9] Stuart[10] and Mc-

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FIGURE 2



FIGURE 1

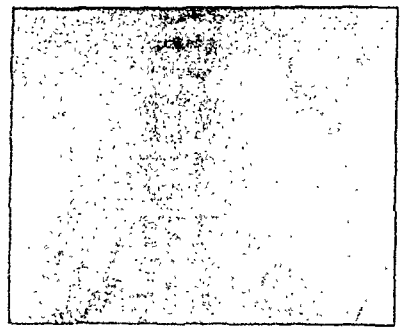
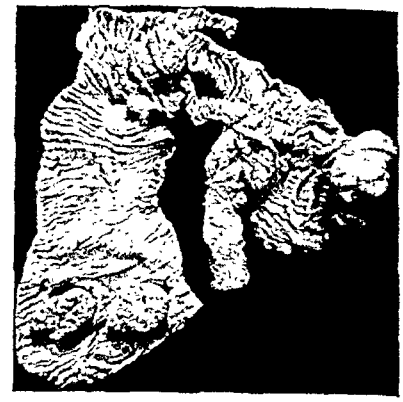


FIGURE 3



Dougall.[11] The literature on duodenal neoplasms was ably reviewed by Ross Golden. Raifford,[12] in reviewing the records of Johns Hopkins Hospital, found eighty-two instances of primary intestinal tumors, seventeen of which were adenomas. Of these, six were found in duodenum, one in jejunum and ten in the ileum. Seventeen per cent gave symptoms but were recognized only at autopsy. In 30 per cent of the cases intussusception occurred. He was the first to mention the possibility of dense shadows in a "scout" roentgenogram occurring in connection with enteric tumors though he gives no specific instances. He also pointed out that achlorhydria in the presence of carcinoma of the small intestine occurs rather constantly and is of diagnostic importance. This view also was concurred in by Waters and Wellbrock.[13] Roentgenologic observations were reported by Wood and Pena;[14] they emphasized the importance of dilated small intestinal coils, large accumulations of barium in the small bowel in the six-hour film, and streaks and smears of barium as indicative of obstruction. Saint,[15] in a study of fifty-seven cases of polypi at the Mayo Clinic, found thirteen occurring in the small bowel. Of these, only one true adenoma was found in the duodenum. Of thirty-two cases of adenomatous polypi, carcinoma occurred in thirteen. Doering states that 45-50 per cent cases of adenomatous tumors undergo carcinomatous changes.

SUMMARY

1. A case of polyposis of the duodenum and the jejunum, undergoing malignant degeneration, with death from intussusception is described.

2. The radiologic aspects of the case are commented upon.

3. A review of the literature relating to the clinical, pathologic and radiologic aspects of the case is presented.

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CONTENTS

SECTION I.—CLINICAL MEDICINE — Page

CHRONIC ULCERATIVE ENTERITIS—*Philip Corr, M.D. and William C. Boeck, M.D., F.A.C.P.* — 161

GASTRIC SECRETION FOLLOWING IRRADIATION OF THE EXPOSED STOMACH AND THE UPPER ABDOMINAL VISCERA BY ROENTGEN RAYS—*Albert M. Snell, M.D. and Jesse L. Bollman, M.D.* — 164

SINGLE GASTRIC POLYP—REPORT OF AN INSTANCE—*Martin G. Vorhaus, M.D. and Arthur E. T. Rogers, M.D.* — 169

RECURRENT "HIATUS HERNIA" SYNDROME OF VON BERGMANN—*Felix Cunha, M.D.* — 170

ABSTRACTS — 173

SECTION II.—EXPERIMENTAL PHYSIOLOGY

AN INVESTIGATION CONCERNING CERTAIN SUBSTANCES REPORTED TO AFFECT THE MOTILITY OF THE GALL BLADDER—*W. L. Voeglin and A. C. Ivy* — 174

THE ANTIPEPTIC INFLUENCE OF GASTRIC MUCIN—*Earl A. Zaus, M.D. and Leonard S. Fosdick, Ph.D.* — 177

ABSTRACTS — 179

SECTION III.—NUTRITION

MORTALITY IN DIABETIC CHILDREN—*Henry J. John, M.D.* — 180

THE EFFECT UPON THE GASTRIC JUICE SECRETION OF VARIOUS COOKED PREPARATIONS OF HADDOCK (MELANOGRAMMUS AEGLEFINUS) AND OF LOBSTER (HOMARUS AMERICANUS)—*A. Alley, M.D.* — 182

ABSTRACTS — 184

SECTION IV.—ROENTGENOLOGY

X-RAY'S CONTRIBUTION TO THE DIAGNOSIS OF THE "ACUTE ABDOMEN"—*William H. Stewart, M.D. and H. Earl Illick, M.D.* — 185

SECTION V.—THERAPEUTICS

CHRONIC ULCERATIVE COLITIS: TRENDS IN ITS PRESENT-DAY MANAGEMENT—*J. Arnold Bargen, M.D.* — 190

ABSTRACTS — 192

SECTION VI.—ABDOMINAL SURGERY

DIVERTICULOSIS AND DIVERTICULITIS OF THE SMALL INTESTINE—*Irvin Abell* — 193

THE CONGENITAL PERICOLIC MEMBRANE SYNDROME, OFTEN MISNAMED CHRONIC APPENDICITIS—A PRELIMINARY REPORT OF OBSERVATIONS—*W. H. Bueermann, M.D., Ph.D.* — 196

ACUTE LIVER DEGENERATION: TREATMENT BY CHOLECYSTOGASTROSTOMY WITH DISCUSSION OF THE CLINICALLY, PATHOLOGICAL AND PHYSIOLOGICAL ACCOMPANIMENTS—*Chas. Gordon Heyd, B.A., M.D., F.A.C.S.* — 203

SECTION VII.—SURGERY OF THE LOWER COLON AND THE RECTUM

...TIS OF THE COLON (WITH ABSCESS FORMATION) INITIATED BY TRAUMA FROM AN ENEMA TIP—*Jerome M. Lynch, M.D., F.A.C.S.*

P. Cowell, M.D.

SECTION VIII.—EDITORIAL

...CATION AND "THE SLUGGISH SYSTEM"

SECTION IX.—BOOK REVIEWS

...ORMIONE—*von Paul Trendelenburg and Otto Krayer (Berlin)*

...DERN ASPECTS OF GASTRO-ENTEROLOGY—*M. A. Arafa, M.R.C.P. (London)*

...ASTRIC ANACIDITY—*Arthur L. Bloomfield, M.D. and W. Scott Polland, M.D.*

...DIETETIC THERAPY IN EPILEPSY—*Eugene Foldes, M.D.*

SECTION X.—AFTER "HOURS"

THE EVOLUTION OF OUR DIET—*Samuel S. Allshuler, M.D.*

SECTION XI.—SOCIETIES, PROGRAMS AND PROCEEDINGS

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AMEBIASIS EXHIBIT AT THE CLEVELAND SESSION OF THE AMERICAN MEDICAL ASSOCIATION

PUBLISHED MONTHLY BY THE SANDFIELD PUBLISHING CO., FORT WAYNE, INDIANA

VOLUME I — MAY, 1934 — ...R II

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CONTENTS

	Page
SECTION I—CLINICAL MEDICINE	
THE PROBLEM OF INFECTION IN GALL BLADDER DISEASE WITH A REPORT ON THE EXPERIMENTAL PRODUCTION OF CHOLECYSTITIS—*Martin E. Rehfuss, M.D. and Guy M. Nelson, M.D.*	759
INTESTINAL GIARDIASIS IN NEW ENGLAND, WITH NOTES ON ITS PATHOGENICITY AND SYMPTOMATOLOGY—*Lee MacPhee, M.D. and Burnham S. Walker, M.D.*	768
FUNCTIONAL AND NERVOUS DISORDERS OF THE STOMACH AND ALIMENTARY TRACT—*Burrill B. Crohn, M.D.*	773
ONE HUNDRED AND SIXTY-NINE STUDIES IN GASTRIC SECRETION DURING THE NIGHT—*Asher Winkelstein, M.D.*	778
CLINICAL NOTES CONCERNING DISTAL ILEITIS AS A MANIFESTATION OF BACILLARY DYSENTERY—*Joseph Felsen, M.D.*	782
ABSTRACTS	783
SECTION II—EXPERIMENTAL PHYSIOLOGY	
THE INHIBITORY EFFECT OF HISTAMINE ON GASTRIC SECRETION—*Armine Alley, M.A.*	787
ABSTRACTS	794
SECTION III—NUTRITION	
VITAMIN "A" AS A PROPHYLACTIC AGAINST THE COMMON "COLD" IN GROUPS OF SCHOOL CHILDREN—*Esther M. Tress, M.A.*	795
ABSTRACTS	797
SECTION IV—ROENTGENOLOGY	
THE DIFFERENTIATION OF CONFUSING SHADOWS IN CHOLECYSTOGRAPHY—*Morris A. Hershenson, B.S., M.D.*	799
ABSTRACTS	802
SECTION V—THERAPEUTICS	
THE TREATMENT OF MASSIVE GASTRO-DUODENAL HEMORRHAGE—*Frank Smithies, ScD., M.D.*	803
ABSTRACTS	807
SECTION VI—ABDOMINAL SURGERY	
"SILENT" CARCINOMAS OF THE LARGE INTESTINE—*E. Lee Strohl, M.D. and J. A. Bargen, M.D.*	808
PORTAL CIRRHOSIS—THE COMBINED MEDICAL AND SURGICAL MANAGEMENT—*Howard A. Rusk, M.D. and Harold G. Newman, M.D.*	810
ABSTRACTS	813
SECTION VIII—EDITORIAL	
ABSTRACTS OF MEDICAL LITERATURE	817
INTRODUCING FRED JENNER HODGES	817
PROFESSOR BOLDYREFF AND THE MAY, 1933, SESSION OF THE AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION	818
SECTION IX—BOOK REVIEWS	
AMEBIASIS AND AMEBIC DYSENTERY—*Charles F. Craig*	819
SECTION XII—"THE CLINIC"	
AN INSTANCE OF SYPHILIS OF THE STOMACH—*V. C. Rowland, M.D. and E. E. Woldman, M.D.*	822
AN UNUSUAL INSTANCE OF PRIMARY MYOSARCOMA OF THE STOMACH WITH RECOVERY FOLLOWING OPERATION—*M. E. Gabor, M.D., M. Tufts, M.D. and W. C. F. Wille, M.D.*	825

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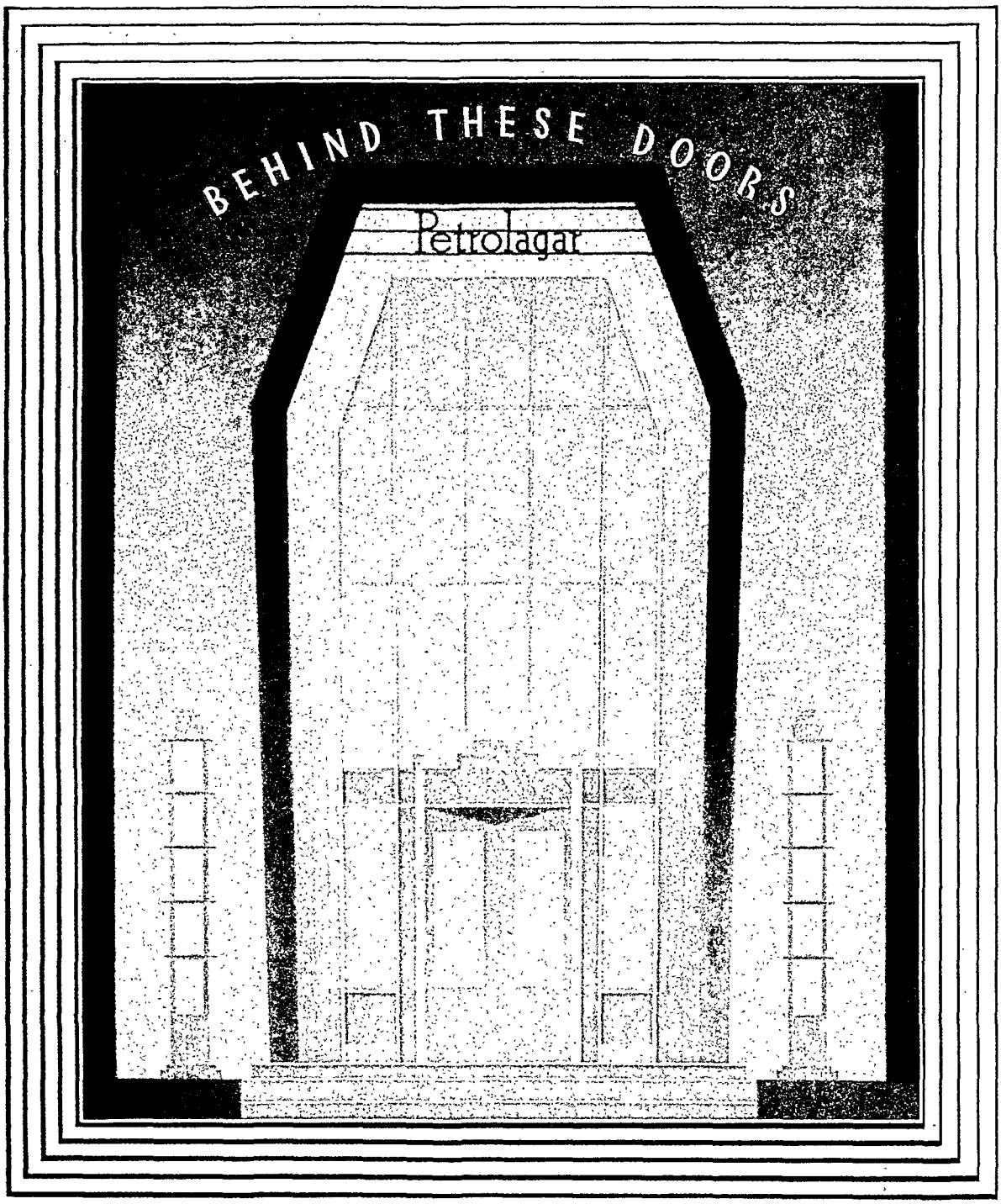
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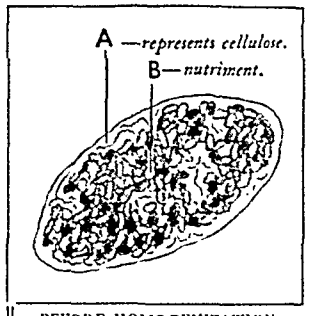
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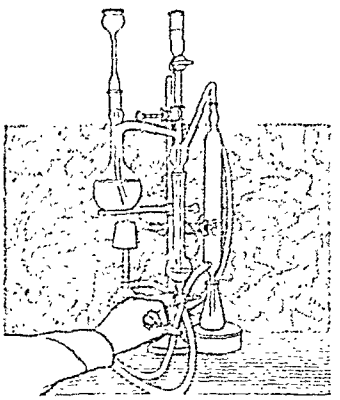
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SECTION I—*Clinical Medicine: Diseases of Digestion*

The Problem of Infection in Gall Bladder Disease with a Report on the Experimental Production of Cholecystitis*

By

MARTIN E. REHFUSS, M.D.

and

GUY M. NELSON, M.D.

PHILADELPHIA, PENNSYLVANIA

THE etiology of gall bladder disease is a problem which has engaged the clinician and the research worker alike. The medical profession has accepted at least several mechanisms by which gall bladder disease can be produced. These mechanisms roughly may be classified as *infection* with its far-flung possibilities both systemic and local. Secondly—*metabolic disturbances* involving the work of the digestive tract, the endocrine system and all those influences which either directly or remotely affect the status of the liver bile and finally, the *mechanical factors*, stasis or any other interference with the normal transit of bile through the biliary tract. It is altogether probable that a disturbance by one mechanism may be associated with a disturbance in the other groups. Vicious cycles, resulting in gall bladder disease, may be infective, metabolic or mechanical, one or all.

In this contribution we are concerned with the evidence favoring the development of gall bladder infection. This evidence is gleaned from the surgical removal of the gall bladder on the operating table, from the bacteriological studies of the excised gall bladder, from the experimental production of cholecystitis in animals and finally, as we shall try to prove elsewhere, a clinical picture more or less characteristic of this condition.

Rosenow, after years of work upon this subject, brought forth the view that bacteria possess an "elective affinity" for different organs and tissues due to properties innate within the bacteria themselves. Proof of this hypothesis is questionable. Many experiments indicate that not every laboratory animal will develop a lesion from an organism which has produced such in other experimental animals of the same species, just as not every person will develop an acute "cold" when exposed to such. The explanation commonly offered is that innate, protective forces are present, the tissue's resistance is too great, the "soil" is not suitable. But, granting that a certain tissue has a suitable "soil", will infection occur if an organism enters? It has been shown that the virulence of many bacteria can be changed by environment. Prolonged growth on artificial media lessens it, successive passages through experimental animals increase it. Rosenow contends that the same organism tends to locate in different tissues when its virulence has been changed. For instance, streptococci, which let us say, affect the tendons in one instance, may, after a few successive animal passages affect the gall bladder, and later the stomach in experimental animals of the same species. In other words, change of environment produces change in virulence; change in virulence produces change in the point of election for lodgement. Theoretically, it follows that although an organ may be receptive to a certain disease-producing bacterium, a lesion need not occur unless the former environment of the bacterium is such as to favor the growth of that organism in this tissue. Experimental work seems to indicate that environmental changes occur in the human body. For instance, the introduction into experimental animals of similar bacteria cultured from the surface and from the substance of the tonsils has produced different lesions. Rosenow believed that their habitat was such that they grew under different degrees of oxygen tension, in conjunction with different numbers and kinds of bacteria and their products. To support this view, organisms grown under different degrees of oxygen tension in the test tube have been observed to behave differently in experimental animals.

In all this work the differences in the natural protective powers of the host, in cultures of the same organism and in the interpretation of the findings in experimental animals have made the investigation difficult and subject to great error.

*From the Frankford Foundation for Medical Research, Philadelphia.
Submitted October 31, 1934

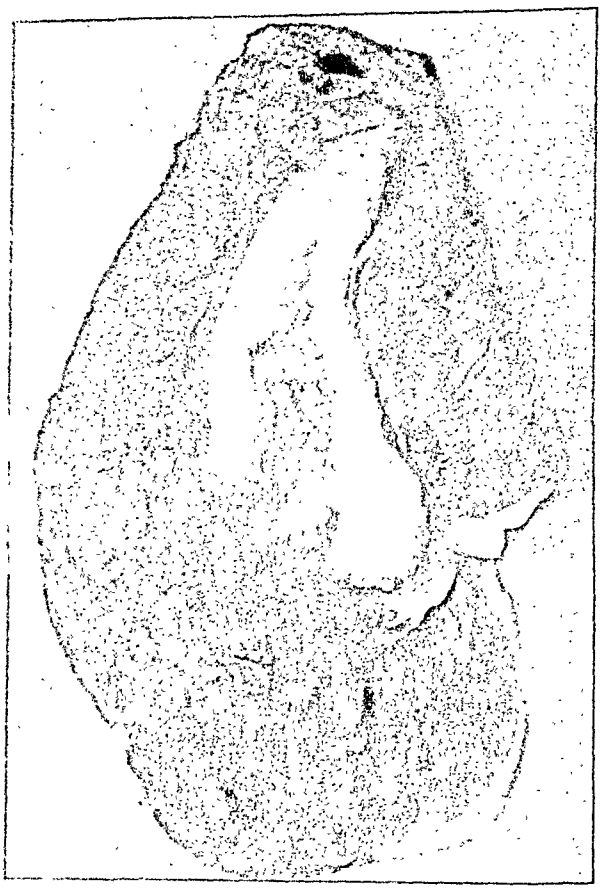


Fig. 1 Chronic Cholecystitis in Rabbit; Tremendously thickened walls. Streptococcus Viridans. Tooth Strain.

But, as time has passed, the evidence of many astute observers has lent support for and against Rosenow's conception. Brown, after investigating the cultures of seventy diseased gall bladders and four peptic ulcers, believed that different strains showed a marked elective affinity for certain tissues. Judd and McKee used one hundred and thirty-two rabbits and injected seventy-two strains of bacteria obtained from diseased gall bladders. Thirty per cent of the rabbits developed lesions of the gall bladder, whereas the highest localization in any other organ occurred in only two per cent. Williams and McLachlan found very little, if any, localizing power in an investigation of thirty-one strains of streptococci and other organisms obtained from diseased gall bladder walls, gall bladder contents and cystic lymph nodes.

In our present state of knowledge, it is probable that all will agree that there are delicate, innate forces in the various tissues of the body upon which depend susceptibility to infection. It has been proven that the virulence of some organisms can be affected by environment. It seems reasonable to believe, and the results in experimental work indicate it to be true, that such changes occur in the human body. The findings from animal experimentation indicate that some strains of bacteria tend to locate in one organ or type of tissue in a large per cent of cases, elsewhere in a much smaller percentage. Whether the determining factor is in the bacteria or tissues or both remains open to question. In such diseases as cholecystitis, where many organisms probably are etiological factors, it seems likely that the "soil" or tissue plays the determining *rôle*.

The consideration of gall bladder disease brings up the question of the bacteriological evidence of infection of the gall bladder or its contents. Boardman, doing experimental work upon fifty-six cases by non-surgical drainage of the gall bladder, compared the cultures from the tonsils and gastric residues with cultures from the various bile specimens taken after stimulation of the gall bladder. Hoping to prevent contamination of the gall bladder specimens, attempts were made to sterilize the mouth and stomach after those cultures were taken by thoroughly rinsing each with solutions of potassium permanganate. He found the bile cultures to resemble those of the tonsils or stomach in from seventy-four to eighty-six per cent of cases and concluded that the method was unreliable. Smithies and others have found a high percentage of positive cultures from bile specimens and concluded that it was probably significant when one or all cultures contained a predominant increase in one type or group of organisms. Cultures obtained by duodenal intubation in our experience as a rule, have organisms similar to those found in the nose and throat.

A group of observers has investigated this question by culturing the fluid content of gall bladders removed at operation. Drennan reported nineteen per cent had positive cultures in a series of one hundred unselected cases. Brown discontinued this method because of the small percentage of positive cultures obtained. Moynihan reported that, in his series of eighty-one cases, approximately thirty per cent had positive cultures; Branch in a series of two hundred ten cases, forty per cent; Rosenow in one series of fifty-five cases, fifty-four per cent. Drennan investigated the effect of bile upon bacterial growth in test tubes and concluded that, in concentrations over seventy per cent, growth was unsatisfactory. Wilkie in a similar manner showed that bile inhibits the growth of streptococci. On the other hand, McKee and Judd found bile in small amounts did not inhibit the growth of streptococci. Drennan and Branch believed their positive cultures came from those cases in which the concentration of the gall bladder bile had been lowered. Here we see fair examples of the extremes in the findings which have appeared in the medical literature. That there are organisms present in the contents of diseased gall bladders, at times, seems proven, but the frequency of incidence is questionable. No doubt the variance can



Fig. 2. Calculous Cholecystitis. Antigen 7. Rabbit No. 15. Non-Hemolytic Streptococcus.

be partly explained by the differences in the concentration of the bile and the pathologic differences in the organs themselves.

Next let us consider some of the findings from operative cases in which the walls of the gall bladder were cultured. Denton discontinued the procedure in his series. Many times, he states, a normal organ gave a positive culture, an abnormal a negative culture. Branch, in a series of two hundred ten cases, reported twenty-five per cent to have positive cultures; Deaver fifty-two per cent (fifty-seven cases), Moynihan thirty-seven per cent (eighty-one cases), McKee and Judd fifty per cent (three hundred cases), Brown fifty-one per cent (seventy cases), Rosenow seventy-nine per cent (sixty-four cases), Wilkie eighty-four per cent (one hundred cases). Here, again, there is extreme divergence in results. How can it be accounted for? The material studied may account for some difference in results. Branch, Brown, Illingworth and Johnson report a much higher percentage of positive findings from the acute cases. Perhaps at times, in a series of cases, gall bladders were cultured which harbored no disease. We know that the contamination of cultures is unavoidable to some extent. Again, certain observers have pointed out that special culture material, prepared under different conditions from the routine laboratory media, give an environment more suitable for the growth of the organisms ordinarily obtained. At any rate, the evidence is convincing that in the wall of the gall bladder, bacteria in some percentage of cases are present, more commonly in the acute than in the chronic cases.

What types of organisms have been isolated? Wilkie reported streptococci in a very high percentage of cases and occasionally bacilli (colon, and Welchii). He described the former as closely resembling those found in pyorrhea, infected, dead teeth, and chronic tonsilitis, which usually are classed in the *streptococcus viridans* group. McKee and Judd reported forty-four per cent of their cases to have green producing streptococci, thirty per cent bacilli of the colon typhoid group, twenty-six per cent staphylococci which most often were thought to be contaminants. They reported the bacilli alone or with the streptococci almost invariably in cases of extensive hemorrhagic cholecystitis and empyema of the gall bladder. Branch found, in his series, colon bacilli in forty-nine per cent of cases, staphylococci in seventeen per cent, streptococci in eleven per cent, dysentery bacilli in four per cent, typhoid bacilli in two per cent, *Bacillus welchii* in eight per cent and mixed organisms in six per cent. He described the streptococci as belonging to the enterococcus group, *beta* hemolytic type, and *alpha* hemolytic type. Brown found the streptococci in seventy-five per cent of the acute cases and in thirty per cent of the chronic; the colon bacilli in fifteen per cent of the acute cases and eighteen per cent of the chronic; the colon bacilli alone in twelve per cent of the chronic cases and with the streptococci in six per cent. The streptococci, he stated, varied; some produced green colonies, others hemolyzed the blood media, still others had different fermentative powers. Rosenow reported, in a series of thirty-two cases, that approximately sixty-five per cent contained streptococci, approximately thirty-seven per cent colon bacilli, and a negligible per cent staphylococci, *Bacillus mucosa, Bacillus welchii, Bacillus fusiformis* and diphtheroid bacilli. The streptococci were alone in over thirty-one per cent of instances and together with colon bacilli in twenty-five per cent of cases. The colon bacillus was alone in slightly more than three per cent of cases and

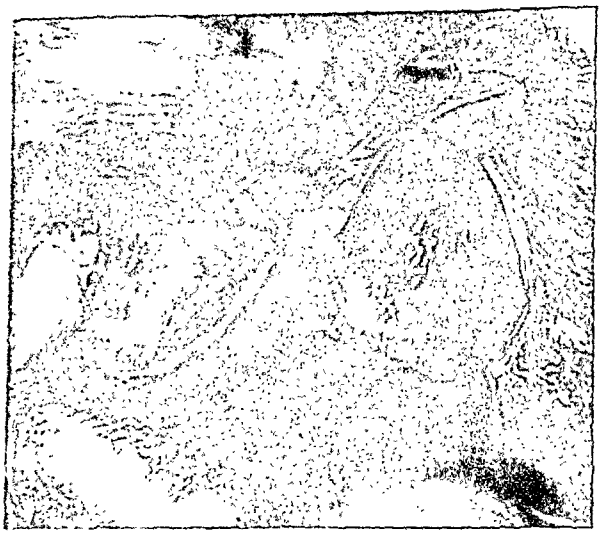


Fig. 3. Chronic Cholecystitis produced by Non-Hemolytic Streptococcic Strain from colon. Filtrate. Rabbit No. 70.

mixed with organisms (*B. welchii*, diphtheroid, and staphylococcus) in twelve and one-half per cent of cases. He described the streptococci as producing "a small, moist, greyish-brown or greyish-green, non-adherent, non-hemolyzing colonies on human blood agar; they produce short chains in liquid media with clumps of cocci closely resembling staphylococci". He believed them to have a rather low virulence and somewhat characteristic fermentative reaction. Magner and Hutcheson found streptococci in thirty-seven per cent of their cases, staphylococci in thirty-seven per cent, colon bacilli in twenty-eight per cent, and other organisms in twenty-four per cent. These investigators divide the streptococci into two groups depending upon whether they have the ability to resist bile and produce cholecystitis or not. Forty-three per cent displayed such qualities. Taylor and Whitby emphasized the frequency with which *Bacillus welchii* was found in a series of fifty cases. Williams and McLachlan found the streptococci which they isolated to be non-hemolytic. Some were enterococcal in type, others salivary, still others *gamma*. By serologic studies they found them to be heterogenous. Again, the reports conflict, but, taken as a whole the streptococcic, colon-typhoid and staphylococcic groups are the constant findings from the walls of surgically removed gall bladders.

It appears that there are two great groups of bacteria found, one resembling those found in the various foci of the head, the other resembling organisms found chiefly in the bowel. The latter group resists bile, thrives in varying degrees of temperature, and is probably the more important of the two groups.

Could the lesions be reproduced by these organisms in experimental animals? The work cited below was work done by the intravenous injection of cultures from the walls of gall bladders removed at operation. Wilkie reported that many cultures produced cholecystitis with great regularity and of a nature in every way similar to that in man. McKee and Judd could not reproduce the lesion with pure cultures of the staphylococcic and diphtheroid groups. They observed that focal lesions occurred in twenty-four hours at times, that chronic, indurated lesions required three to five weeks to develop, that colon bacilli differed from streptococci in that usually they produced muco-purulent bile with necrosis of the wall in a shorter time, that a gram negative bacillus, often mixed with the streptococcus, sometimes tended to produce gangrenous cholecystitis. They used forty-one strains containing streptococci in large numbers, sixty-eight per cent of which localized in the gall bladder. From thirty-one other strains in which streptococci were absent or present in small numbers, lesions in the gall bladder were produced in less than seventeen per cent. Forty-five per cent of seventy-eight rabbits developed lesions of the gall bladder from the injection of the forty-one strains, only nine per cent from the thirty-one. The highest incidence of localization elsewhere was in the joints (two per cent). Localization was ten times higher in this group than in another series in which strains from various sources other than the gall bladder were injected. Branch, in experimental work upon twelve animals, reported that four developed gall bladder lesions out of proportion to lesions elsewhere and that these were produced separately by the colon bacillus, *streptococcus hemolyticus*, the typhoid and dysentery bacillus. Rosenow reported that eighty per cent of forty-one animals developed lesions of the gall bladder. He used twelve strains of streptococci. In another group of three hundred ninety-six animals into which he injected bacteria from various sources other than from the gall bladder, only three per cent developed lesions in that organ. In his first group, localization occurred in the skin (two per cent), muscles (seven per cent), joints (seventeen per cent), intestines (seventeen per cent), stomach and duodenum (twenty-nine per cent), kidneys (five per cent), lungs (five per cent), myocardium (two per cent), endocardium (ten per cent). In another series, he reported a staphylococcus as having marked affinity for the gall bladder, that mixed cultures of colon bacilli and streptococci localized in the gall bladder of forty-six per cent of eleven animals, that three cultures of colon bacilli which were obtained with streptococci originally showed no election for the gall bladder, that two cultures of colon bacilli where streptococci had not been present originally had a marked tendency to localize in the gall bladder. Williams and McLachlan reproduced the lesion with the colon bacillus in one instance (used six strains); with streptococci in one instance and possibly another (thirty-one rabbits

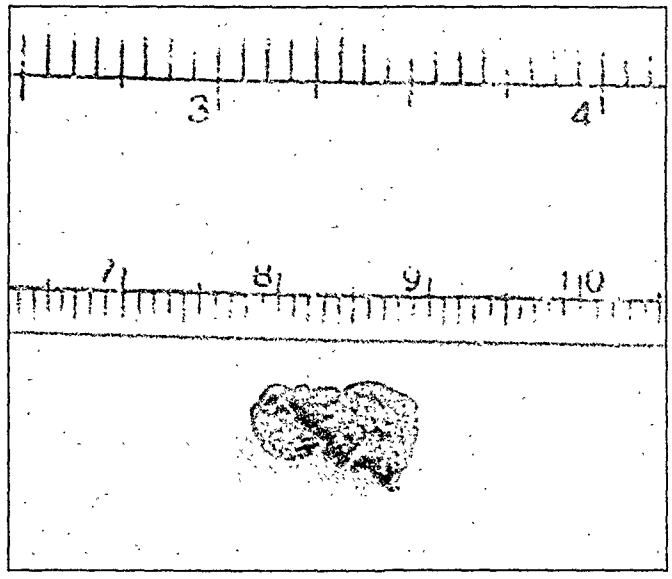


Fig. 4. Gall stone from experimentally produced cholecystitis. Hemolytic streptococcus strain. Antigen 69—isolated from gums (Cholecystitis patient.) Rabbit No. 132.

and thirty-one strains of streptococci used); but they were unable to produce it with the *staphylococcus aureus*. Magner and Hutcheson could not reproduce it after nineteen experiments with streptococci. But they were successful in practically every attempt when the bacteria were injected directly into the gall bladder walls. Rosenow, Brown and others have reported the recovery of the organisms from the lesions produced.

This brief survey on experimental lesions leads us to believe that the streptococci, the colon-typhoid group and occasionally other organisms can produce cholecystitis; that localization is not definite, but probably partial to this one organ in contra-distinction to lesions produced by organisms taken at random.

Before leaving this phase of the subject, let us consider briefly that condition described by Moynihan and W. J. Mayo, the so-called "strawberry gall bladder". The whitish, punctuate areas which gave rise to the name have been proven to result from deposits of cholesterol esters in the epithelium and the areolar tissue of the mucosa. This lipoid substance may be seen in varying degrees from minute deposits in the epithelial cells, to large deposits which may fill and distend the loose tissue of the villi. Starling investigated the degrees of concentration of the various constituents of the gall bladder bile. He reported that the concentration of cholesterol was much less than were some of the bile salts. This may be interpreted as being circumstantial evidence that cholesterol is absorbed by the mucosa. Boyd found pathologic evidence of infection associated with such cases and suggested the possibility that the infection might produce an obstruction to the absorption of cholesterol by the lypmhatics and blood vessels resulting in the deposits subsequently. A large per cent of Moynihan's cases on this subject lends support to that view. Wilkie reported streptococcic cultures from the wall and cystic lymph nodes in all cases examined. McKee and Judd obtained twenty-nine per cent of positive cultures from the gall bladder walls in a series of sixty-five cases. Usually these were from cases with complicating factors, such as stone, and they concluded that unless such factors exist they are usually sterile. Rosenow reported four cases of which streptococci were obtained from cultures either of their stones or walls. Illingworth could not reproduce the lesion by increasing the blood cholesterol unless the gall bladder walls were infected. Williams and McLachlan obtained positive cultures from the gall bladder walls of four of eight such cases. The evidence is too scant to arrive at a just opinion although it seems possible that infection may play an important *rôle*.

Most interesting and important observations have been made concerning the *relationship of foci of infection to cholecystitis*. The frequency with which they were associated, the occurrence of attacks of acute cholecystitis following acute tonsillitis and the like, the favorable results following the removal of foci of infection aroused in the investigator a suspicion that there might be an unknown relationship between the two. It was observed that frequently a streptococcus very similar to those found in pyorrhea, dental abscesses and chronic tonsillitis had been recovered from the gall bladder wall and that intravenous injections of these had produced cholecystitis. Workers began to explore different foci in attempts to discover organisms similar in their cultural and elective characteristics to those found in the gall bladder walls. Rosenow cites an example of his work, in which a patient had chronic cholecystitis. After the extraction of infected teeth there was no improvement; so the tonsils were removed, resulting in marked improvement for one year. Cultures from tonsils given to one rabbit and two dogs produced lesions of the gall bladder, pancreas and duodenum. Afterward, the patient recomplained and three unerupted roots of teeth were found and removed. Cultures of these contained a green producing streptococcus which, when injected into laboratory animals, showed similar localizing powers. The patient improved. Rosenow also used vaccines made from organisms of associated diseased foci with, at times, distinct benefit to the patient. Brown reported investigations of a similar nature and concluded that the elective affinity of strains from tonsils for the gall bladder of animals indicated strongly that cholecystitis commonly is a blood-borne infection from a focal source. This viewpoint is of great importance and has been stressed by clinicians and experimental workers alike. To correct a condition one must seek the cause and then remedy it. This source of infection may be a diseased sinus, pulpless tooth, a prostatitis or,

for that matter, any active infected focus. Rosenow points out the great danger of having pulpless teeth which so frequently are infected, of infection about the apices of the teeth not associated with pain. The lack of pain he claims means that free drainage was established from the lesion into the circulation which accounts for the absence of swelling with the symptom of pain.

TABULAR REVIEW OF 4,395 CASES OF CHOLECYSTITIS

Bacterial Study in 2,162 Cases—Exclusive of Rovsing's 530 Cases

AUTHOR	No. Cases	Walls Culture	Contents Cultures	Stones Present	Stones Cultures	Acute No. Cases	Acute Cultures	Chronic Cases	Chronic Cultures	PREDOMINATING ORGANISM in Order of Frequency.
Bullock	270		58	..	..	..	..	..	..	B. Coli 49%; B. Typhosis 10%; *Staphylococci* 12%; *Strep. Non-Hem.* 3%; B. Coli and S. Non-Hem. 4%. Others Cases Collected from 1889 to 1925 at Johns Hopkins.
[illegible]	240	53		94	27	57	42	153	11	B. Coli Staphylococcus Streptococcus
[illegible]	70	36	.	.	..	20	15	50	21	Streptococcus B. Coli
[illegible]	17		Cholecystitis is not usually the result of an acute process but rather as a result of mild infection—slowly affecting different layers of the gall bladder. Chronicity is favored by the anatomy and histology of the organ, which predisposes to stasis and obstruction.							
Deaver (1)	57	30 (24 pos. cystic nodes, 6 neg. cystic nodes).	7		..	..	..	..	..	
Deaver (2)	903	No Bacteriological study made.		451	CONCEPTION—Modern Opinion Primary Hepatitis often preceded by appendicitis.					
Denton	433		.	188	Failure to demonstrate lesions primarily bacterial in origin leads author to conclude that factors other than infection (mechanical and circulatory) are necessary for explanation of the majority of lesions commonly observed in the gall bladder.					B. Coli or Gram pos. Bacillus in 4 out of 91 paraffin sections.
Drennan	100	84		..	..	..	..	..	..	B. Coli Staphylococcus Streptococcus
Feinblatt	400			240	A pathological study leads one to believe that the role of infection in the causation of cholecystitis has been greatly overestimated—whilst the importance of the metabolic and mechanical factors has not received due consideration.					B. Coli Predominating in pus of 20 (Empyemia) cases
Friedlein	132	73 of 96 exam.	62 of 132 exam.			..	.	..	..	B. Coli
Gordon-Taylor and Whitby	50	41	16	50	14	..	..	..	..	B. Coli 30%; Strep. Faecalis 28%. B. Welchii 18%; Staphylococcus 18%. Others 4%.
Illingworth	100	62	40	62	7	12	10	88	52	Streptococcus B. Coli Staphylococcus
Johnson	100	31	32	66	16	20	13	78	18	B. Coli Staphylococcus Streptococcus
Judd	200	98	28 of 197 exam.	107	24 of 61 exam.	.	..	..	..	Streptococcus B. Coli Staphylococcus
Kelly	210	113					.	..	..	B. Coli B. Typhosis Staphylococcus Aureus
Mayo and Hutchison	200	178		119			.	..	..	Streptococci (Typical 12—5%) B. Coli 26% (Atypical 17%) Staphylococcus 26%. Others 19%.
Mayo and Hutchison		.	34 of 105 exam.		..		..	.	..	B. Coli 17 9%. Streptococci (Typical 2-8%) Staphylococci (Atypical 3-7%) Others 5-6%.
Moynihan	81	30	25				.	..	..	
Rovsing	76	53 of 64 exam.	39 of 64 exam.		57 of 92 exam.		..	..	.	Streptococcus B. Coli
Rovsing	530			530	216	..	..	.	..	
Williams and McLachlan	105	50 of 96 exam	43 of 93 exam	47	14	4	3	93	43 of 84 exam.	B. Coli Enterococcus Staphylococcus B. Welchii and others
Wilkie (1)	50	6	6	.	..	..	..	..	..	Streptococcus B. Coli From 4-5 Cystic Glands—43 Streptococci
Wilkie (2)	100	84			..	..	..	..	..	Streptococcus Viridans.



Fig. 5. Subacute Cholecystitis produced by B. Coli Infection.

AUTHORS' INVESTIGATIONS

At the Frankford Foundation for Medical Research we have spent considerable effort upon the question of experimental cholecystitis. Through the courtesies of Drs. B. L. Crawford and C. J. Bucher, of the Jefferson Hospital, organisms were obtained in pure cultures of hormone broth from areas clinically believed to be diseased, nasal discharges, abscessed teeth, gums, tonsils, bile, urine, prostatic secretion, colon walls. Subcultures on agar media were preserved at refrigerator temperature as sources from which subsequent cultures were obtained. It was our desire to produce, if possible, chronic lesions more like one would expect to occur from a focal area which probably throws into the blood stream at varying intervals a small number of organisms or their by-products. So we placed one platinum loop of the cultures into approximately 5 c.c. of hormone broth and measured the number of organisms in terms of hours of growths at 37 degrees C. such as six, eight, and twenty-four hours' growth. Small, ascending amounts were injected into rabbit's ear veins usually beginning with .02 c.c. of the six-hour culture. These were repeated in larger doses once or twice a week depending upon whether or not there were signs which would lead one to believe that the rabbits were sick, such as loss of appetite and weight, temperature changes, joint disease. Frequently, it was necessary to discontinue after two, three or four small injections; then again, the dose reached 3 c.c. of a twenty-four-hour culture. Prior to each injection the cultures were examined and smears were made in order to be positive that contamination had not occurred. The rabbits were autopsied after two to ten months, except in the case of a few which died or were sacrificed because of extreme illness.

TABLE I

Organism	No.	No. Rabbits Used	No. Diseased Gall bladders	Organisms recovered from bile.
B. Coli	5	7	4	5
B. Pyocaneous	1	2	1	2
B. Mucosus Capsulatus	1	1	0	0
Strep. Hemolyticus	2	2	1	1 (1 ?)
Strep Non-Hem.	4	66	13	7 (1 ?)
Strep. Viridans	2	2	1	0 (1 ?)
Staph. Aureus	1	8	2	3 (2 ?)
Total	16	88	22	17 (5 ?)

?—Organism with some slightly different characteristic from original

Figures 1 to 7 are representative reproductions of gross and histologic findings from these autopsies. They illustrate the engorgement of blood vessels, distension of the gall bladder, thickening of the wall and the leukocytic infiltration. Such were the findings in varying degrees of those considered to be diseased gall bladders. Up to the present time more than thirteen hundred rabbits have been used since work began at the Frankford Foundation. Several hundred animals which had not received bacterial injections were autopsied; none of these presented gall bladders similar to those considered to be diseased.

From Table I one observes that, with one exception, diseased gall bladders were found after the injections of a variety of organisms obtained from various focal areas. Twenty-five per cent of the rabbits were so affected. Organisms were recovered at times from the bile of gall bladders believed to be grossly normal; in the latter opinion we may have been mistaken. In five instances the organisms recovered differed in some degree from those injected and were, therefore, considered questionable. From this study one cannot help but be impressed by the variety of bacteria capable of producing experimental cholecystitis.

Routes of Gall Bladder Infection—How may the gall bladder become infected? Primary infection is rare. As we breathe, eat and drink various bacteria, conceivably it may occur, especially when a non-infectious agent such as a stone has produced local mucosal trauma or occlusion of its ducts, but far more important are those infections secondary to foci of infection, such as the bowel, teeth, tonsils, sinuses.

Let us consider the possible routes by which bacteria may enter this organ. Occasionally surgeons and pathologists have produced evidence showing that infection had extended from a neighboring organ. Diseased appendices situated high in the abdomen have been reported in which there was every reason to believe that infection



Fig. 6. Cholecystitis produced by Streptococcus Nonhemolyticus. Bowel Strain. Rabbit No. 71.

had spread directly to the gall bladder. At times the same may be said of penetrating, infected, peptic ulcers. However, these are rare findings but without doubt account for the occasional case.

Then there is that possibility, so long taught and believed, of organisms going up the common or down the *hepatic ducts* into the cystic duct and gall bladder. Bond showed that the intestines have a retrograde current, that charcoal administered from below could be found in the gall bladder. The foreign element necessarily had to travel up the ducts. Gall stones formed about foreign bodies have been reported. Barium has been reported to fill the gall bladder following oral administrations. Moreover, in a series of cases of cholecystitis probably fifteen to twenty-five per cent have very little or no free hydrochloric acid. The gastric germicidal function is impaired thereby, with the result that infectious organisms can pass into the duodenum with each gastric evacuation and possibly go up the common bile duct if the sphincter of Oddi be open. Moynihan reported sixty-six per cent of his cases of achlorhydria to have positive cultures of the gall bladder bile, only twenty-eight per cent of those with normal or increased HCl content. But on the other hand, Rosenow was unable to produce a lesion experimentally by the direct injection into the lumen of organisms which were known to have produced cholecystitis when administered intravenously. Others have shown that normal gall bladder bile inhibits bacterial growth. One would expect the ducts to be infected oftener and to a greater degree than is the gall bladder, which is not the case, were this the route. Cultures from the gall bladder bile gave a smaller percentage of positive cultures from those from the gall bladder wall, findings which one would not expect if the infection came by way of the ducts. Unless there be some disturbance in the concentration of bile this route seems unlikely in the majority of cases.

Turning to the descending route, bacteria may come from the liver by way of the hepatic and common ducts. The liver is thought to have great germicidal power although Patey and Whitby have shown its inefficiency as a bacterial filter. The portal vein takes large numbers of bacteria to it for destruction. On the one hand, the spleen, an organ whose duty is thought to be to filter out organisms and send them to the liver, on the other hand the appendix, an organ which is said to be the most common site for infection in the abdomen, are notable sources from which the portal system may receive bacteria. Moynihan cited three cases of cholecystitis associated with hepatitis, the most marked changes being about the portal tracts, as possible evidence to support this route. Granting that bacteria do escape the destructive forces of the liver, the inhibitory power of the bile upon bacterial growth, the failure to produce acute cholecystitis by direct injection, the reports of hepatic abscesses associated with normal gall bladders, indicate this to be an unlikely route unless there is some disturbance in the bile concentrating mechanism.

Next there is the *lymphatic route.* The lymphatics of the liver and gall bladder are thought to have free communication. In a series of thirty cases, E. A. Graham reported associated inflammatory lesions of the liver in every case. Taylor, in Moynihan's series of eighty-one cases, found an associated hepatitis. Moynihan believed that usually there was an associated antecedent hepatitis, citing as proof the marked frequency in his series in which the outer coat of the gall bladder was more seriously affected than was the inner (in eighty-one cases sixty-three to eighteen). Patey and Whitby found no evidence of spread by this route after the injection of India ink and carcinomatous tissue, the latter being known to spread extensively by way of the lymphatics. Surely, there can be no doubt of the possibility of this route but, as Walton points out, the hepatitis may be secondary to the cholecystitis. In view of the hepatic changes being most marked about the gall bladder this conception would seem more likely.

Finally there is the *hematogenous route.* The venous blood empties into the portal system. For infection to spread backward from it necessarily would mean that along its path somewhere infec-



Fig. 7. Microphotograph. Gall Bladder Wall Rabbit No. 180. Streptococcus Viridans from throat of a patient with calculous cholecystitis.

tion had occurred in its walls with resulting vascular change. This is very unlikely. Turning to the cystic artery we have blood which could have passed through almost any focus in the upper half of the body and much of the lower half. It is conceivable to imagine that bacteria may in this manner be swept along with the blood current. A large amount of experimental work supports this view. Repeatedly in laboratory animals by various observers bacteria have been injected into the blood stream and lesions of the gall bladder alone or in associations with other organs have occurred. Not only organisms from diseased gall bladder walls but from various foci throughout the body gave demonstrable lesions in the gall bladder alone, and many times they were demonstrated by stains within the tissues. The demonstration of chemical cholecystitis at times when Dakin's solution was injected into the blood stream of laboratory animals seems to agree with this view.

Of necessity this has been a very brief survey of a large volume of work done upon this subject. Deliberately we have omitted a discussion of various phases such as serum agglutination tests, fermentative and detailed cultural characteristics of the micro-organisms. In a separate communication certain phases of this nature have been considered. The bacteriologic investigations of the cystic nodes were avoided because the results appear to coincide in a great measure with those of the gall bladder walls. Too, there is that objection that infection of the cystic nodes does not indicate, necessarily, infection of the gall bladder.

CONCLUSIONS

1. In a composite review of two thousand one hundred sixty-two cases of cholecystitis studied bacteriologically following cholecystectomies, more than forty-five per cent yielded positive cultures from the gall bladder wall, more than twenty-nine per cent from the contents of the gall bladder.

2. Many bacteria were obtained, but most common were the streptococcic, colon-typhoid and the staphylococcic groups.

3. From an experimental standpoint cholecystitis can be produced by a variety of organisms. There appear to be no specific bacteria.

4. Foci of infection appear to play the primary etiologic *rôle* and may be divided into two regions, the head and bowel.

5. The elective localization of bacteria as an hypothesis is open to question.

6. The route by which bacteria reach the gall bladder in the majority of instances appears to be by way of the blood stream.

7. In general, from this study we are inclined to believe that almost one-half of the cases of gall bladder disease seen clinically are bacterial in origin.

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Intestinal Giardiasis in New England, With Notes on Its Pathogenicity and Symptomatology*

By

LEE MacPHEE, M.D.

and

BURNHAM S. WALKER, M.D.
BOSTON, MASSACHUSETTS

GENERAL CONSIDERATIONS

THAT intestinal infestation with *Giardia (Lamblia) intestinalis* is not rare among inhabitants of the temperate zones, is evident from a brief consideration of the literature on this subject. Lyon and Swalm,[26] reviewed, in 1925, 3,200 cases, gleaned from a literature of 118 titles, of which less than half the instances were from the tropics. Boeck,[2] in a study of 50 admissions at the Children's Hospital in Boston, observed an incidence in children of 14 carriers among 80 miscellaneous medical admissions. Teitge,[48] reports from his observations on coal miners in the Ruhr district, that of those presenting gastro-intestinal symptoms, 21 per cent were infested with giardia.

While it is true, Boeck[2] has observed the instance as reported above, very infrequently we hear of giardiasis in New England. The literature gives us no facts regarding it and, from our own figures, we can not approximate those of Boeck.[2] Where his frequency practically is 21 per cent, in our own series, discovered in routinely examined cases at the Evans Memorial, we have found only six cases in a series of 732 patients where a routine bile drainage was done; this is but an incidence of .82 per cent. Our group is comprised of a miscellaneous number of children and adults, male and female, and we believe the incidence showed in this group gives a truer picture of the disease in New England than do the higher figures. Association of giardia with other parasites has been reported a number of times. One noteworthy case, carefully studied by VonBrand,[4] is that of a symptomless carrier of both giardia and entamoeba histolytica.

It would seem to be desirable, as a matter of routine, in those patients who present symptomatology such as we cite below, to do microscopic examinations of both the duodenal bile and the examination of the stool and upon fresh, warm specimens. Most of our cases of giardiasis have been discovered during routine examinations; it is evident that there are many instances, perhaps the majority, where giardia may be detectable in the stools or the duodenal contents of patients who exhibit negligible or no indication of any clinical disturbance caused by the presence of the parasite. Similar occurrences have been discussed by Paulson and Andrews,[33] Peterman,[35] Heubner,[19] Dalsace,[11] Maxcy,[28] Scheidel,[39] Smithies,[45] and others.

All writers who have considered the question of giardiasis at all agree that this infestation is not accompanied by eosinophilia. One of Simon's[42] cases had 6 per cent eosinophiles, but this was explained by a concomitant infestation with *Trichuris trichuriae*. The only reported uncomplicated case exhibiting an eosinophilia is that of Anisimov;[1] there the eosinophiles ranged from 6 to 12 per cent, but the total white cell count was normal. It seems reasonable to assume, in the face of the many cases of giardiasis where eosinophilia was absent, that in Anisimov's case a factor other than infestation by this protozoön was operative.

In a very appreciable number of instances reported in the literature, the presence of giardia has been associated with certain fairly well-defined symptoms. Often, those symptoms are indicative of disturbance of the liver, gall bladder and bile ducts. Anisimov[1] reports a case with jaundice, enlarged liver and pain in the right hypochondriac region. Cases with the typical syndrome of cholecystitis are reported by Kantor,[21] Felsenreich and Satke,[14] Morenas,[32] Grilli,[18] Heubner,[19] Coia and Gavrila,[10] Deschiens,[12] Chantroit,[6] Petukhov,[36] Goia and Haltza,[16] Knighton,[22] Winkler,[55] vonRehren,[37] Westphal and Georgi,[52] Schill,[40] Boeck,[2] Smithies,[45] and Golob.[17]

A smaller number of reported cases show a symptomology varying from the biliary type.

*From the Evans Memorial (Massachusetts Memorial Hospitals) and the Boston University School of Medicine.
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Beck[2] reports a case resembling cholera. Finley[15] describes a case of pellagra which he attributes to the interference with absorption of digested food by large numbers of sessile giardia on the cells of the intestinal mucosa. Tsuchiya and Andrews[30] had the opportunity of observing a case of "laboratory infection" with giardia, exhibiting epigastric pain, nausea and fatigability. These symptoms were not present before the accident infestation and were absent after the victim had been rendered free from giardia by stovarsol treatment. Labbé reports a case with early biliary symptoms, which terminated fatally due to a pericaecal abscess. Savolin presents two cases where giardia appears to have caused an anemia of the Addisonian type. Luger[24] believes that a particular type of enteritis results from association in the intestine of giardia with the spirochaete and fusiform bacillus of Vincent. Silva[41] records perforation of the sigmoid as terminating a colitis attributed to giardia infestation. Penso[34] does not recognize a true biliary type of disturbance caused by giardia, but classifies its symptomology as "intestinal" (colitis, with acute dysenteric exacerbations), "non-intestinal" (anemia and neuroses), and "mixed". His study is based on 100 cases.

In children, who appear to be more susceptible to giardia infestation than do adults, the symptomatology is apt to be diverse. Miller[21] had indicated the existence of the chronic type of enteritis apparently the result of such infestation; often it simulates coeliac disease. McClendon[20] believes that giardia is definitely pathogenic for children, and, clinically is accompanied by tenderness of the colon, often associated with constipation, nervousness, fatigue and loss of appetite. Peterman,[35] in addition to reporting symptomless instances of giardiasis, mentions children who experienced enteritis with giardia infestation. Zahorsky[37] believes that there is a definite "giardia syndrome" in children; protracted diarrhoea, gradual distention of the abdomen and retardation in growth. Mathieu[27] reports a case of chronic *prurigo atrophulus* in a child of seven years, which had been present since early infancy, which was relieved promptly by treatment freeing her of giardiasis.

DISCOVERY, MORPHOLOGY AND HABITAT

It appears proper here to correct some historical misstatements which have appeared and reappeared in many articles on this subject. The discovery of giardia should properly be credited to Leüwenhoek; he observed the organism in his own stools (Boeck,[3] Heubner[19]), and not to Lambl. The report on the first American case was that of Stiles,[47] who, in 1902, described the experimental infection of a guinea pig with material obtained from a child treated in Baltimore by the late Dr. John Hemmeter.

It seems unnecessary here to discuss in detail the morphology of giardia. This subject is well treated in textbooks of parasitology and clinical pathology, and particularly so in the articles of Wenyon,[51] Golob,[17] Wezler,[50] and Boeck.[3]

The question of the parasite's habitat is a vexed one, and deserves some further discussion. That, in the majority of cases, giardiae are limited, as far as free adult forms are concerned, to the duodenum and jejunum, seems well established (Paulson and Andrews[33]). There is a growing accumulation of evidence that, at times, the organism may invade the bile ducts and the gall bladder. In the biliary type of clinical giardiasis, numerous investigators have observed the protozoön in material obtained by the duodenal tube, in fractions of the duodenal contents generally believed to come from the gall bladder or bile ducts. In Anisimov's case, the organisms were found both in the duodenal contents before "stimulation", increased numbers were seen after administration of pituitrin to stimulate gall bladder contraction. Similar findings were noted in Labb's fatal case. Toullec,[49] holding a more radical position than most investigators, thinks that intestinal giardiasis is but an episode in vesical (gall bladder) giardiasis. He bases his opinion on the frequent finding of the organisms in "A", "B" and "C" bile, and on instances (not described in detail) where they were found in the excised gall bladder. Morenas[32] summarizes the evidence for the giardiasis of the biliary tract as follows:

1. "B" bile often contains more organisms than does "A" bile or duodenal contents.
2. The organisms are seen entangled in mucus flocculi or spirals, commonly present in gall bladder bile. (Felsenreich and Satke[14]).
3. Giardiae have been found in "B" bile while no cysts have been observed in the stools.
4. Pituitrin causes contraction of the gall bladder and increases the number of giardiae seen in the duodenal contents.
5. Giardiae have been actually recovered from the contents of gall bladders removed at operation in three instances; two reported by Smithies,[45] one by Westphal and Georgi.[52]

The last piece of evidence appears to be beyond refutation; the number of cases thus proved is, however, very small. Morenas admits that there also have been instances where giardiae were demonstrated in "B" bile, but not in the gall bladder at operation. Paulson and Andrews[33] do not believe that the finding of organisms in "B" bile necessarily indicates their presence in the gall bladder. Carnot and Gaehlinger[6] believe the magnesium sulphate may appear to increase the concentration of giardiae in the "B" bile, while actually it only serves to dislodge them from the duodenal mucosa. The use of pituitrin, however, is free from this objection. All observations on removed gall bladders have failed to show sessile giardiae; the cases summarized by Morenas were of organisms free in the fluid. The value of the intravenous arsenicals in the treatment of giardiasis is believed to be the result of the excretion of arsenic by way of the bile (Kantor[21]).

CASE REPORTS

The following cases were instances where the giardiae were discovered during routine examination; they are presented briefly to illustrate the diversity of effects of the parasite. In four of these patients we believe the symptomatology was dependent upon the giardiasis, while in the fifth case (a child), apparently the host was a carrier.

Case No. 237008—(Removal of gall bladder and appendix without alleviation of symptoms; later, finding of giardiae). A young woman, age 28, admitted to the Massachusetts Memorial Hospitals in September, 1933, with complaints of *constipation* (since typhoid 12 years previously), *epigastric pain* and *"heaviness"* not definitely associated with meals (duration 5 years). Previous antiluetic treatment. Wassermann and Schwartz-McNeill tests negative. Leucocytes 10,400, no eosinophilia. Widal negative. Bass-Watkins, weakly positive.

A *cholecystogram* was interpreted as indicating "abnormal peritoneal attachments of gall bladder with probable cholesterosis of mucosa".

Operation: The gall bladder and appendix were removed. The report of the pathologist was "healed appendix with complete obliteration. Early acute exacerbation of a chronic cholecystitis". The patient was discharged on the twelfth post-operative day.

In March, 1934, the patient returned with the original complaint of obstinate constipation.

Physical examination revealed nothing noteworthy aside from marked *fetor ex ore*. Routine laboratory examinations, including a gastro-intestinal X-ray series, yielded normal findings. Motile giardiae, 10 per high power field, were found in a specimen of duodenal contents.

Case No. 188688—(Appendicectomy and second exploratory laparotomy; marked digestive disturbances). Male, age 39. Referred to Evans Memorial for endocrine diagnosis. He was found to have a marked degree of hypothyroidism. He knew beforehand that he had a giardiae infestation, the duration of which was not known.

His *major presenting symptoms* were an ichthyosis and inability to take certain foods. At the age of 21 he had had his appendix removed. A year later he developed the skin condition (considered as an ichthyosis, and possibly of arsenical origin), and associated digestive disturbances. "Since 1910 patient has had a bothersome skin trouble which has been diagnosed as ichthyosis and arsenical dermatitis. This involves the entire body, burns incessantly, worse during day, does not itch. The skin is hypertrophic and exfoliates considerably in scales. There has never been any rash except as generalized erythema, transitory and recurrent. This seems to depend largely on ingestion of definite foods, namely, fats, fruit, milk and cream. The condition always has cleared up in the summer, but is worse than ever this year and did not clear up during the past summer. There has never been burning until this year, and never has itched. The first attack was sudden; patient got up in morning "in a shower of scales". This cleared up rapidly and did not recur to any extent until 1916. . . . During this time, patient had been bothered with abdominal pain following ingestion of milk . . . no nausea or vomiting . . . fruits do not cause pain . . . yellow coloration of skin following taking of meat, but can take liver. Cream and milk also cause the yellow color. . . . Slight posterior pharyngitis noted on overindulgence in milk or cream. . . . Believes skin reaction caused by fats . . . epigastric pain follows eight hours after a meal, especially milk or cream . . . (apparently, a striking instance of food allergy).

Physical examination demonstrated pallor, emaciation, with yellow tint of skin and sclerae, no evidence of disease of nose, throat or sinuses. Liver not enlarged, but there was tenderness in the gall bladder region. (The patient had had an exploratory operation of the gall bladder region ten years previously with "nothing abnormal" found). The skin was dry, scaly and hypertrophic except on the hands where it was atrophic.

Examinations of *urine* and *blood*, including the Van den Bergh reaction, were negative. The *basal metabolic rate* was depressed 25 to 33 per cent (4 determinations). Free HCl was present in the stomach. Numerous giardiae were observed in the duodenal contents.

Endermal reactions (positive for celery, spinach, oat, bean, rice, buckwheat); did not show any hypersensitiveness to milk, and to numerous other articles of food.

Case No. 203861—(Three surgical episodes; marked neurosis). Single woman, age 27.

First seen in 1929 (June), complaining of pain in the right lower abdominal quadrant. *X-ray and physical examination* suggested early tuberculous infection of both lungs, as well as a pathological appendix. The medical and surgical attendants agreed that the lung condition was of greater moment than was the abdominal; the patient was advised to take a long rest in the country and attempt to put on weight.

Further abnormalities which should be noted were: a tendency to chronicity of mild infections (e. g. styes becoming abscesses requiring considerable surgical attention); chronic frontal sinus infection; chronic night and morning cough, with thick yellow expectoration; low substernal pain, dyspnoea and palpitation with mild exertion; night sweats; poor appetite; eructations of gas; upper abdominal discomfort promptly following meals; burning sensation in throat, and sometimes vomiting. There was apparently extreme constipation; no diarrhoea. The digestive disturbance mentioned began about a year before this entry. There had been, in that period, a loss of 25 pounds in weight.

Examinations of blood, urine and sputum were negative. X-rays of the gastro-intestinal tract, including oral cholecystography, were negative. A chest X-ray demonstrated a dilated left auricle, hazy infiltration of both lungs. The patient was afebrile.

In October, 1929, she was readmitted, still complaining of attacks of nausea and vomiting, and steady dull pain in the right lower abdominal quadrant. There was definite pain on hyperextension of the thigh.

Appendectomy was performed, and she was discharged 14 days after operation. The pathologist's report was "slight chronic appendicitis". Previous to discharge a chest and X-ray examination gave no indication of pulmonary tuberculosis. *Six* sputa were examined for tuberculosis with negative results.

In November, 1929, she was briefly admitted to the neurological service, with a complaint of vomiting since her operation. After 18 days of nutritional therapy she was discharged as "improved".

Late *in February, 1932*, she appeared at the Evans Memorial for diagnostic study. "For the past year and a half (she) has complained of sharp pain in the epigastrium, radiating around to upper right quadrant and under right shoulder blade. Attacks of pain may be very dull, lasting for about a day at a time; . . . after noon or evening meal is often taken with attacks of nausea and sometimes vomiting . . . no jaundice or hematemesis; . . . bowels regular, no clay-colored or black stools; . . . has lost 28 pounds in one year". On the other hand "The attacks of pain in the epigastrium are sharp, leaving her sore for three or four days. There have been 11 or 12 of these attacks; those of the last month were referred to the right scapular region; occasional diarrhoea". She is reported by the examiner as being "extremely nervous".

Physical examination revealed an undernourished woman, with a small area of dullness and rale below the right clavicle; tenderness and spasm in the right upper quadrant and epigastrium. The liver was palpable, one centimeter below the costal margin.

Urine examination was negative. *Blood examination* revealed leucocytosis of 12,300 (1 per cent eosinophiles). Chemical examination of the *duodenal bile* gives practically

normal findings, the furfurol number being slightly low. No microscopic examination of the duodenal contents was made at this time. A stool report was negative for occult blood, parasites and ova. The *X-ray diagnosis* was visceroptosis, adhesions about hepatic flexure and sigmoid colon, chronic cholecystitis with perivesicular adhesions.

At operation (March, 1932), congenital abnormal peritoneal attachments joining duodenum and hepatic flexure were cut away, the gall bladder removed, and adhesions about the old appendix scar broken up. The surgeon reported the gall bladder as "essentially normal", and stated a belief that most of her trouble arose from the abnormal peritoneal attachments. He piously stated "The patient should be relieved of her pain in this locality". She was discharged on the 24th post-operative day, surgically recovered but "weak and no appetite".

The pathologists' report was "Mucosa of the gall bladder is intact. Villous processes tend to be low and atrophic. The wall shows a marked fibrous thickening, particularly in the region of the serosa and is infiltrated throughout with lmyphocytes, plasma cells and endothelials." Pathological diagnosis: chronic cholecystitis.

In June, 1933, the patient returned for an exploratory laparotomy on account of abdominal pain, poor appetite, occasional fainting attacks, irregular and excessive menses. *At operation* a small uterine fibromyoma was excised and a mesenteric lymph-node removed for examination. Adhesions of the omentum to the old appendix scar were cut. The pathologist reported the mesenteric node as tuberculous.

In July, 1933, she returned to the Evans Memorial for observation, still complaining of abdominal pain. At this time, the finding of giardiae in the duodenal contents was made. In one instance, the parasites were bile stained.

Case No. B-2342—(No symptoms clearly attributable to giardiae). A boy, 11, referred to the Evans Memorial for endocrine study, an ichthyosis which had persisted since early infancy; a maladjusted "problem" child.

No symptoms or signs were observed referable to the abdomen or digestive tract. The examination of the duodenal contents was made in the course of the study; motile giardiae were found (30 per high power field) in the specimen taken in the fasting condition. Two specimens taken after stimulation of bile flow relatively were free from the parasites. This would seem to indicate, together with the lack of symptoms, that the habitat of the parasites in this case strictly was duodenal, without infestation of the bile ducts.

Case R. B.—(Abdominal pain, relieved by treatment of giardiasis). Man, age 47. Had typhoid in childhood, appendicectomy at age 25. In 1925, for a short period, had dull epigastric pain and was relieved by taking food between meals.

For the last two or three months has had short attack of right upper quadrant pain. For ten days before consulting the senior author this pain had been "steady".

Physical examination essentially was negative except for pain and tenderness over the right, upper, quadrant and sensitiveness over the epigastrium. On pressure, pain seemed to radiate downward, there being no marked spasm. Giardiae were found in the bile sediment. The Graham test was negative. Analysis of the duodenal bile showed a marked decrease in bile acids with corresponding decrease in the cholesterol and alcohol-soluble and insoluble pigments. The values for these constituents in the "C" bile practically were normal.

Treatment: The patient was put on thymol, 30 grains t.i.d. for a period of three days, after one day of active catharsis. He was given magnesium sulphate, 5 c.c. saturated solution every other day. After one week the pain and discomfort disappeared. At the end of one month the patient's weight increased from 152 to 157 pounds. There was absolutely no epigastric or right upper quadrant tenderness. and examination of the duodenal bile showed increase in the constituents of the "B" bile, with no giardiae in the sediments (June 29, 1934).

Can any helpful conclusions be drawn from the rather chaotic literature concerning giardiasis, and from highly variable symptomatology found not only in our cases, but equally in those of the majority of previous investigators? We believe there are certain guiding principles which should be emphasized.

1.—*Giardia is clinically pathogenic.*—Whether or not the combined work of Fantham and Porter[13] and of Tsuchiya and Andrews[50] constitutes a complete, technical fulfillment of Koch's postulates might be open to question. Yet we are confronted with the fact that the literature contains a steadily growing number of reports of patients, who are sufficiently ill to call for hospitalization, and often for exploratory surgery, where either before or after operation giardia is found, and no other abnormality of enough moment is demonstrable to explain the conditions. In many cases, treatment aimed at the reduction of the number of giardiae has alleviated or removed the symptoms. Few complete cures (proved by prolonged and repeated examinations for the organism) are reported by any method of therapy.

2.—*The symptomatology is predominently intestinal.*—This is to be expected, since the intestine is believed by the majority of investigators to be the chief *locus* of infestation. The effect on intestinal motility appears to be the most usual disturbance, giving the symptoms of constipation or diarrhoea, or an alternating syndrome. Secdary undernutrition and possibly anemia, rather vague neurotic manifestations, and, at least one report, of frank pellagra, appear to be sequential to the intestinal disturbances. The dermatological symptoms, if indeed these have any connection with the parasitic infestation, possibly might be considered as the consequences of deficient liver function, or nutritional anomalies "conditioned" by the presence of the protozoön.

In the more severe cases of giardiasis the presenting symptom-complex is more biliary than intestinal. In reading the case reports, a familiar syndrome begins to take shape, comprising in almost all instances nausea and upper abdominal pain of varying degrees of severity; less frequently jaundice; liver enlargement and a tender or palpable gall bladder. Some degree of disturbance of the motility of the gall bladder, demonstrated by the Graham test. tips the balances in favor of a diagnosis of cholecystitis. The gall bladder is removed, the pathologist usually observes some evidence of chronic inflammation, the patient makes a good recovery from the operation, but the original presenting symptoms may recur. Further study then reveals the presence of giardia, usually by examination of the duodenal contents, less often, by finding cysts in the stools.

3.—*Cholecystectomy does not cure giardiasis.*—The evidence is good (Morenas[32] and Smithies[45]) that giardia may invade the gall bladder, but is

equally good that this is not of frequent occurrence. The contention of Toullec[13] that the gall bladder is a reservoir of giardia infection, causing recurrent intestinal episodes, may apply to the African cases upon which his observations are based, but is not borne out by the work of any other investigator. The probabilities are that next to the upper small intestine, the bile ducts are the most common *locus* of the parasite, and only rarely and intermittently the gall bladder, and then only in conjunction with other *loci*. Cholecystitis secondary to, or arising independently of giardiasis may require surgical treatment; such treatment is or is not a part of the management of the parasitosis.

4.—*Giardiasis is not an exotic condition.*—We have already commented upon reports from investigators from most of the American medical centers, and from numerous foreign countries, which reports indicate a by no means negligible incidence of giardiasis. Children are more prone to this infestation than are adults, although children appear less likely to suffer the more severe manifestations. Some surprise was expressed by earlier investigators, *e. g.*, Smith and Matthews,[13] at the discovery of giardiasis in people who never had traveled in out of the way places, but such surprise is no longer justified.

5.—*Giardiasis should be considered in all cases where cholecystectomy for chronic cholecystitis or cholesterosis, in the absence of definite evidence of gall stones, seems indicated.*—While it is not feasible to recommend the passage of the duodenal tube in all patients who exhibit vague intestinal symptoms, it does not seem out of line to recommend that a sample of duodenal contents be examined microscopically before resorting to major surgery. The examination should include samples taken both before and after stimulation of gall bladder contraction with magnesium sulphate, oleic acid, pituitrin or other cholecystekinetic substances. Absolutely fresh material in the warm stage must be examined. The microscopic examination may be of aid in diagnosis apart from the possible discovery of giardia; in case giardia be found, experience seems to dictate that, in the majority of instances, the surgical treatment should be postponed and the results of antiparasitic measures awaited.

While the purpose of medical treatment of giardiasis is the complete removal of the organisms, the more usual result has been diminution of their number, with usually relief from the presenting symptoms. The forms of therapy have been varied, including the arsenicals, thymol, emetin, salines, bismuth compounds, duodenal drainage and lavage, and combinations of these agents and procedures.

We found that the thymol treatment, as advised by Smithies, gave us a good result in one case treated. Saturated solution of magnesium sulphate introduced into the duodenum also proved efficacious in destroying the organisms, particularly when at temperature of 105°-110° F.—the thermal death-point of most protozoa (de Rivas). It is difficult completely to eradicate the protozoön. We find on frequent investigation that regrowth occurs if the patient is left untreated for any appreciable time. Outside of the measures mentioned with the number of cases we have observed, we feel that our own experience is insufficient to permit us to enter into a critical discussion regarding merits of various therapeutic agents. For a summary of the present-day views on treatment Golob's[17] recent paper should be consulted.

SUMMARY

1. Giardiasis is not a rare condition.

2. Its pathogenicity varies from zero to the production of severe intestinal and biliary symptoms, with occasional secondary nutritional, neurasthenic and possible dermatological effects.

3. A frequently-observed syndrome in patients, here and abroad, is one suggesting chronic cholecystitis or cholesterosis.

4. Cholecystectomy does not relieve the above syndrome in the presence of giardia infestation. Cholecystostomy, with long-maintained drainage and accompanied by the introduction of protozoacides through the drainage tube offers possibilities. Antiparasitic treatment has been in many cases a means of relief.

5. It is recommended that microscopic examination of duodenal contents be done prior to operation for chronic cholecystitis or cholesterosis, especially in the absence of definite evidence of gall stones.

6. In the absence of other indication for immediate cholecystectomy, it is recommended that antiparasitic treatment be given a trial if giardia be found.

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Functional and Nervous Disorders of the Stomach and Alimentary Tract*

By

BURRILL B. CROHN, M.D.
NEW YORK CITY, NEW YORK

THE title, "Functional and Nervous Disorders of the Alimentary Tract", is itself imposing and covers a wide latitude of symptomatic disturbances, of conditions of visceral imbalance, of emotional and neurotic upheavals and suppressions sufficient to intimidate the most facile speaker or fluent clinician, be he a Charcot, a Weir Mitchell, or a Freud. Put into one scale of a gigantic balance all the cases of ulcer, of gall bladder diseases, and of cancer, and put into the other arm of the scale all those who are suffering from alimentary neuroses, anxieties, phobias and visceral functional disturbances, and the latter arm will descend with its overpowering gravity of numbers.

The magnitude of the problem, and its quality, can better be grasped if one were to enumerate the variety of conditions, their protean manifestations and the diversity of their clinical pictures. Nervous esophageal spasm or true cardiospasm *(achalasia)*; merycism or rumination; gastric atony, pylorospasm or duodenal stasis; spastic constipation, intestinal atony with flatulence, nervous diarrhea; one mentions as the more common of the motor imbalances. *Anorexia nervosa*, bulimia or disordered or abnormal appetite; gastric anacidity or hyperacidity and hypersecretion; mucous colitis, comprise some of the secretory disturbances. We are actually confronted with a diverse group of secretory disorders that bespeak, all of them, a throwing out of balance, an incoordination, of the smooth normal counterplay of vagotonic and sympatheticotonic factors in the control of the alimentary tract. Secretion, its volume and quanity; motility, delay, the control of the various sphincters, peristalsis, antiperistalsis, absorption, these innumerable functions take place normally, rhythmically, with unerring exactness as the result of the superb interplay of the stimulatory vagus or the para-

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sympathetic system and the inhibitory activity of the sympathetic gaglionated cord. This even balance may be, in the neuroses, upset by a psychic shock (affecting a subnormal mental or emotional system), a suppression of desires, an anxiety, an unfulfilled want. The obvious manifestation is frequently a functional disturbance of the alimentary tract, or, as one more euphemistically styles the condition, "an autonomic nervous system imbalance". Back of the disorder is, however, the psychic factor, for the autonomic nervous system is automatic in its daily activity, it is not within the conscious control of the cerebrum or the higher centers, yet it is not impervious, is far from being uninfluenced by those same psychic factors that lead to the pure neuroses.

Gastro-intestinal neuroses are gastric and intestinal and abdominal only in their mode of manifestation; they are anxieties, hysterias, somatic neuroses, neurasthenias and hypochondriases in the truest sense of the word as known to every psycho-neurologist.

Or, let us consider in the more limited sense only the simple gastric or intestinal neuroses. Herein are to be included the nervous air swallowers, the hosts that complain of fictitious pains and burning sensations, of aching epigastric voids, or fullness after meals; of those who have anxiety neuroses, of fear of disease, of carcinophobias, of hysterical vomiting.

Be the manifestation a motor or a sensory disorder, call it autonomic imbalance, or a gastric neurosis, the mechanism essentially is the same, the inferior mental makeup usually handicapped by an impoverished heredity, meeting in conflict an insurmountable obstacle offered by his or her environment. The abdomen is truly "the sounding-box of the emotions".

THE ANATOMY OF THE NEUROTIC PERSON

With what kind of an individual are we dealing? Usually timid, afraid, lacking in self-confidence; subject to emotional instability; or, reticent and suppressed, unable to grasp the hard facts of life or unwilling to accept them, uncertain about the conduct of the past, worried and harried about future events, unable to fit himself into the harsh inequalities of life, out of sympathy with his fellowmen, with family or domestic relations, unequal to cope with his love life or solve his sex problems, such is the psychic or mental anatomy of the individual likely to be a prey to a neurosis.

Physically he is usually underbuilt, only fairly well nourished, often of the so-called enteroptotic constitution of Glenard, with cold moist palms, rapid pulse, anxious mien; with a spastic colon, exaggerated peripheral reflexes, often complicated by a hypersensibility to pain—such is his physical status. He enters the room anxiously or distrustfully, he produces a ream of paper covered with closely written notes, plus a list of questions; he is repititious, vague, unable to express himself clearly, confused as to facts; he always feels that he is not being given sufficient time and attention, and suspects always that he is being misunderstood or unsympathetically handled.

Such an individual comes through childhood and adolescence without nervous manifestations, for the neuroses in the school age are few and far between, and adolescence is a period of protection and parental affection. With the advent of adult life, the individual first faces his stark environment, and between the ages of 18 and 28 years one sees the beginning of the greatest number of neuroses. A woman is happy and well, married with love, and bears her first-born. The child takes sick and sleepless nights are followed by convalescence. Soon one sees the onset of neurotic symptoms in the mother, a furtive hunger, belching, constipation, pains, insomnia. The men, facing the hard economic conditions of the depression, the women worrying over the financial straits of their men-folk or their own living problems, the complicated disharmonies of family life, the care of children, the dependent parents; the sex problems of the young, the frustrations of the adults; the boredom of marriage, the late awakenings of love in women, and the innumerable and varied problems of the individual in conflict with his material and emotional environment —these are the factors that originate the neurotic mishaps.

HEREDITY AS A FACTOR

Students of the neuroses have aptly pointed out the important *rôle* of heredity as an underlying factor in the etiology of functional and nervous complaints. Alvarez was probably more damned than commended when he coined, in a recent article, the title, "Insanity Equivalents and the Gastro-Enterologist". In order to emphasize the influence of bad heredity in generating neuroses, he pointed out that in 1928 state institutions which housed the insane, the imbecile and the epileptic were caring for one out of every 380 of the population. Add to this those who had been at some previous period similarly interned, those confined in private institutions, and add again those members of the population and families who are borderline cases, the emotionally unbalanced and uncontrolled, the insomnias, the milder depressions, and the incomplete neurasthenias, and one may easily say that Alvarez does not exaggerate when he quotes the figure of one per cent as representing that part of the population which is emotionally and psychically unfit. In taking the clinical history of a patient suffering with a neurosis, a few questions regarding the heredity of parents and grandparents often will throw a luminous ray on the misgivings of the presenting patient.

THE MODERN ECONOMIC FACTOR

The most important single factor in the production of the neuroses of today is the disordered economic situation. A few years ago when money came and money went easily, the consulting room of a physician was crowded with well-dressed

women and affluent men, thinking and nursing emotional, often sex, problems. With necessity out of the way, the game of finding and fighting sex conflicts and suppressions was *au fait;* and Freud wrote and founded a popular school of analysts. Today, with poverty at the door, love may not fly out of the window, but is relegated to a subordinate position while the problem of rent, bills, credit and life necessities assumes a primary place, not only in the family councils, in the business hours, but in the subconscious mind of the patient who, already by heredity, by temperament, and by mental constitution, is below par and barely fitted to face the fight for survival.

THE DIAGNOSIS AND RECOGNITION OF THE NEUROSES

The differentiation of the neuroses from organic visceral disease is one of the most difficult problems in clinical medicine. Let him, who is proud of his acumen and experience as a physician, survey, from year to year, his own record in this respect, and his pride may take, *will* take, a severe fall. With his eyes wide open to the problem, with much experience with the world, people and moods, and with years of clinical training and knowledge, no one is immune to, at times, mistaking organic diseases for the neuroses, or of falsely interpreting neurotic symptoms in terms of pathological states.

A male patient of 34 years complains of severe abdominal pain after meals; he has lost some weight, is distressed by food. He presents himself with reports of two radiographic examinations, both of which are said to be negative for organic disease. The patient is highly emotional; he cries throughout his examination; sleeps poorly or not at all, declines food and states that his economic *status* gravely is imperiled and a source of momentary alarm. The etiological factor, economic, is present, the behavior is characteristic, the negative raidographs confirm the suspicion of a neurosis. But the downward clinical course, represented by loss of weight, warns loudly of too final or too hasty a conclusion. A third radiographic study reveals a large niche of a benign gastric ulcer, with a second superimposed lesser curvature crater in the proximate area. Bed rest and a strict Sippy diet, reinforced by gastric intubation, result in cure. In the presence of cramps, or of the complaint of severe pain, particularly in a patient insensitive or subsensitive to pain, beware the diagnosis of a neurosis. Too many X-ray plates are read by less experienced radiographers as negative, which are really positive; too bad that the specialty of gastro-enterology has not yet reached radiography. Radiology is still open to anyone who can wheedle the credit to buy an apparatus, training or no training. The fluoroscopy and plate reading of a difficult gastro-intestinal case calls for an extreme degree of technical accuracy, fluoroscopic experience, and clinical knowledge properly to interpret the findings. At that, the responsibility for the eventual diagnosis rests with the clinician, not with the radiographer.

A patient of 38 years, male, has lost a few pounds of weight, is mildly distressed after meals and belches; he suffers no abdominal pain. He is too worried about the reorganization of his business to spare much time; he apologizes for the vagueness of his symptoms and attributes his slight indisposition to irregular meals and much worry. The clinical impression is one of a gastric neurosis or of a functional disturbance of secretion and motility from psychic overstimulation of the vagus gastric innervation. The obvious, however, was the most dangerous diagnosis; only the loss of weight and a slight facial pallor warned of a too hasty conclusion. Radiographic examination made as part of an office routine revealed a neoplasm of the gastric antrum. At operation, not six weeks after the onset of symptoms, a carcinoma of the body and antrum, with lymph node involvement high along the lesser curvature, was noted. Fortunately, a physiological subtotal resection was successful. Young cancer, or cancer in an early stage, is not a painful disease; in the silent areas of the stomach, away from the sphincters, it is almost mute. Almost, but not quite, and those few mild symptoms of distress, belching and discomfort, are identical with those voiced by every neurotic individual. Again, with the help of the X-ray, the differentiation is possible, but how often, after a first, even a second, and occasionally in my own experience, a third radiographic examination, the negative report is reversed by the clinical course or by subsequent studies. Youth is no bar to alimentary carcinoma; on the contrary, the neoplasm in the relatively young is inversely proportional in severity to the age of onset.

A young woman, married, who had borne children, complains of indigestion, distress after meals, loss of appetite and flatulence. She is apparently unemotional, is controlled, and submits readily to a radiographic routine study. A gall bladder full of stones is readily observed. Cholecystectomy follows as a natural procedure. Following the operation the symptoms immediately recur, now associated with severe vomiting, not of retained food, (no gastric stasis is demonstrable), but of vomiting in the fasting state, and vomiting after even a small meal. A thorough study fails to evince evidence of a pathological state. Now a psycho-analytical study is made and exposes a marital dysharmony, lack of spiritual domestic felicity, a suppression of normal sexual instincts and gratifications. It becomes readily obvious, though rather tardily, that those gallstones, accidentally discovered, were really silent gallstones, that the symptoms were manifestations of a neurosis, that the operation, though logical, was fruitless. The experience with this woman is not an isolated one; numerous similar instances can readily be cited. Gallstones are

negative report for suspected carcinoma of the stomach or of the colon, particularly of the sigmoid-colon and rectum, is not final or conclusive.

The most difficult diagnosis to make, in all abdominal medicine, is that of a neurosis. The diagnosis of ulcer, cancer, cholelithiasis, is made or unmade readily and by simple direct steps; the positive conclusion is acceptable and final to the patient and to the physician; treatment is satisfactory and brings gratitude from the patient and self-satisfaction to the physician. The diagnosis of a neurosis is indirect and negative, is made only after a series of expensive and futile performances and tests, all of which are expected to be negative, all of which are costly to the patient and end with a conclusion which leaves the patient often resentful, doubting, unconvinced and with his psychic problem back on his own hands.

For, if the diagnosis is one of organic disease, the patient feels justified in his judgment in having consulted the physician and trustingly resigns himself for medical care with the expectation of relief. But if the dagnosis is of a nervous or functional disturbance, the problem is turned back upon the patient, who must find his own means for his own cure; true, he has his physician's friendship and advice and experience to guide him. But the patient must alter his own methods of living, decide not to worry himself sick over his failing business, teach himself resignation over a disappointed love affair, accept the defection of his children with stoicism, or teach his wife, or her husband or lover the new code of manners, fidelity, control of temper, and the first principles of affection, cordiality and mutual respect.

TREATMENT

Which is easier, to prescribe a Sippy diet and an alkaline powder and rest for a gastric ulcer, or to sit for an hour and discuss diet, habits, sleep, work, residence, worry, family relations, etc., etc., with a depressed nervous semi-invalid?

The instructive understanding of a neurotic individual and his neurosis, the treatment of functional disturbances, back of which are mental strains and unhappy incidences, is a strain and task on the doctor, one which calls forth, in order to be successful, all of his patience, his innate charm and character, his sympathetic understanding of life in its vicissitudes, and his entire array of clinical experience and scientific knowledge.

The gastro-intestinal neurosis or functional disturbance is often in the patient's mind entirely a question of diet. One must listen carefully and patiently to a thousand questions regarding every article of food. In spite of campaigns of education on diet and the advertisements of new brands of vitamin foods, and the health columns in the daily news, people do not know how to eat or discriminate in their meals. The appropriate diet, in kind, in quality and in time distribution through the day, requires a skilled hand and implicit acceptance.

Fatigue, physical and mental, are at the base of most nervous complaints. More play, more recreation, change of scene, vacations, and sleep, "beloved sleep", are primary elements in any such cure.

Should we spare soporifics to one suffering from insomnia? Should one prescribe sedatives of codein and the barbiturates for these neurotics because of the fear of habit formation? Sedatives, strong sedatives, are to a neurotic or functional disturbance what a plaster cast is to a fractured patient. One would not dream of allowing a broken limb to leave the office without immobilization; one should neither leave a distracted, sleepless, exhausted person to face the days with distress, or the long nights without refreshing repose. I never spare sedatives, and I know of no addict for whom I could be held responsible.

In the good days, business men could be forced to suspend business activities, to recreate in the South, to take rest cures, or travel for health. Women welcomed a stay in a sanitarium or hospital, a Weir Mitchell cure, Carlsbad or Vichy, or the Riviera. In these times of economic distress, emotional and personal, the problem of treating the unfortunate functional or nervous semi-invalid is particularly difficult, since most of these measures call for money, time and leisure.

The one single powerful means at the disposal of every physician, of every general practitioner, is his capacity for understanding, for sympathy and advice. The beloved physicians of history have had those qualifications that made them successful in handling large numbers of patients, most of whom we can be sure were nervous and timorous; Hippocrates, Galen, Boerhaave, Sydenham, and in our time, William Osler. Educated, with natural charm, with culture and learning, with patience and tact, they cared for and comforted and prescribed for the massed group of unfortunates. Not in the medical schools, nor in the clinic, nor in the hospital wards, can such qualifications be acquired, but by studying the lives and characters of such outstanding physicians, by emulating their finest traits, by simulating their social and literary culture, and by the acquisition of the arts can we, as clinicians first, and then as physicians, prepare ourselves to face the care and treatment of the neuroses.

Hippocrates, in "The Physician", said, "The physician, who is also a philosopher, approaches the divine"; and in the "Precepts" he says, "Where love of mankind is, there is also the love of art".

acidities were estimated, and in others only the acidity. The presence of food, bile and mucus was noted. Free and total acidity were determined in the usual clinical manner using Toepfer's solution and phenolphthalein as indicators. Pepsin was estimated by the Mett tube method.

MATERIAL STUDIED AND RESULTS OF OBSERVATIONS

There were 62 cases of duodenal ulcer, 29 cases of gastric ulcer, 17 cases of gastric carcinoma, 32 cases with partial gastrectomy for ulcer, five cases with gastro-enterostomies and 20 controls. Practically all of these cases were adult males.

Controls: Twenty cases were studied. The composite curve is given in Figure 1. Nine or 45 per cent did not reveal any free hydrochloric acid. All had normal free acid (20 to 45 free acidity) in the usual day oatmeal gruel, Rehfuss fractional test meal. In those with free acid, the peak of the curve was reached at 9 o'clock. As a rule, food residues were found in the 7, 9, and 11 P. M.

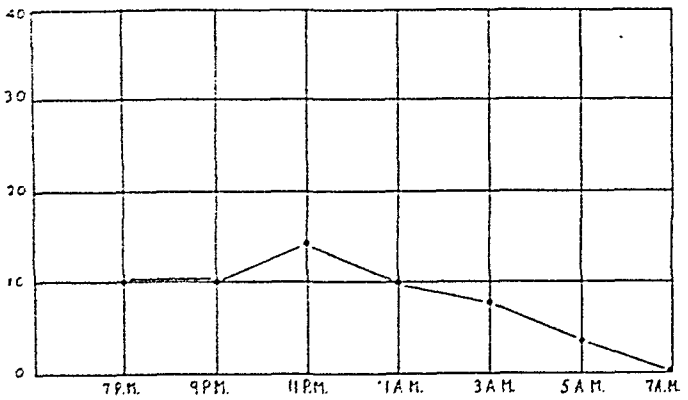


Fig. 1. Composite nocturnal curve of free hydrochloric acid in 20 controls.

aspirations. Bile was seen frequently in the 1, 3, 5, and 7 A. M. samples. The quantities of secretion were small, seldom exceeding 15 c.c. in the whole night.

Duodenal Ulcer: Sixty-two patients with uncomplicated duodenal ulcer were studied. The composite curve is given in Figure 2. Considering 20-40 normal, 40-60 moderately high, and over 60 a markedly high acidity, 80 per cent showed a marked hyperchlorhydria, 12 per cent a moderate hyperchlorhydria, and 8 per cent were normal. The peak of the curve in 34 per cent of the cases was reached at 1 A. M. and in 30 per cent at 9 P. M. This corresponds roughly to the usual periods of night pain in duodenal ulcer. The presence of food and bile was recorded in 30 cases. In 25 cases food was present at 7, 9, and 11 P. M. In these cases bile appeared in the other specimens. The other five cases revealed neither food or bile. No increase in mucus was noted in any case. The amount of secretion was estimated in 18 cases. These averaged a total of 113 c.c. for the seven specimens. The peptic activity

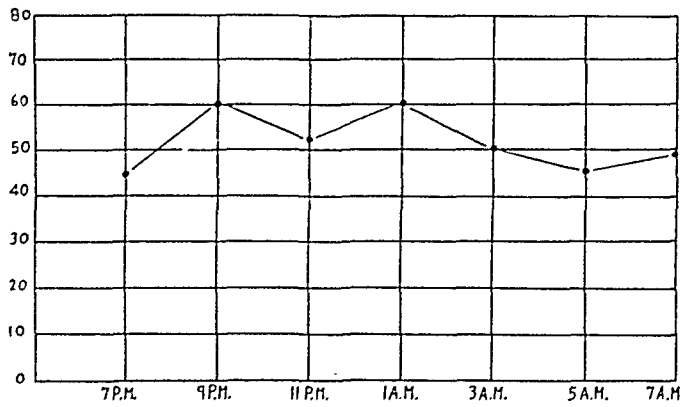


Fig. 2. Composite nocturnal curve of free hydrochloric acid in 62 duodenal ulcers.

in 16 cases averaged a digestion of 3 mm. in Mett's tubes.

Gastric Ulcer: Twenty-three patients with uncomplicated gastric ulcer were studied. The compositive curve is given in Figure 3. Forty-four per cent had a marked hyperchlorhydria, 12 per cent a moderate hyperchlorhydria and 44 per cent were normal. Apparently twice as many patients with duodenal ulcer as with gastric ulcer have a nocturnal hyperchlorhydria. This is also true of the day fractional test meals (8). The peak of the curve was noted at 11 P. M. in 40 per cent and 9 P. M. in 20 per cent of the cases. The quantities of secretion and the peptic activity were identical with that of the patients with duodenal ulcer. Food usually was present at 7, 9, and 11 P. M. Bile, however, was noted only once.

Gastric Carcinoma: Fourteen patients with gastric carcinoma were studied. The composite curve is given in Figure 4. Fifty per cent had an achlorhydria throughout the night. Two had a normal curve and five had a small amount of free acid in the first three tubes. The amount of mucus, blood and total acidity was large in all. In 50 per cent of the cases, the quantity was increased (140 c.c.) and in the other 50 per cent, the quantity was very small (14 c.c.). Pepsin was absent in four cases and averaged low (1.8 mm.) in the others. These findings parallel closely the day fractional curves.

Jejunal Ulcer After Gastro-Enterostomy: Five

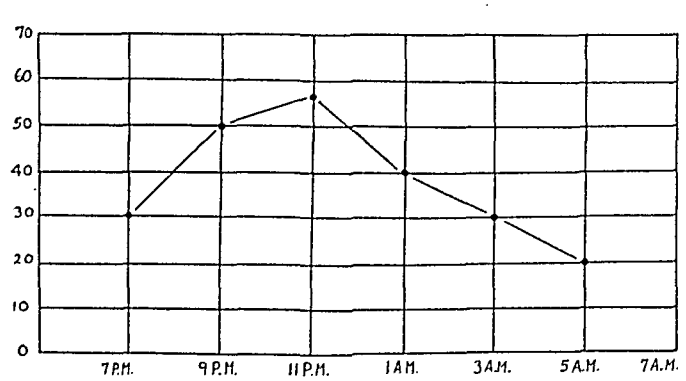


Fig. 3. Composite nocturnal curve of free hydrochloric acid in 23 gastric ulcers.

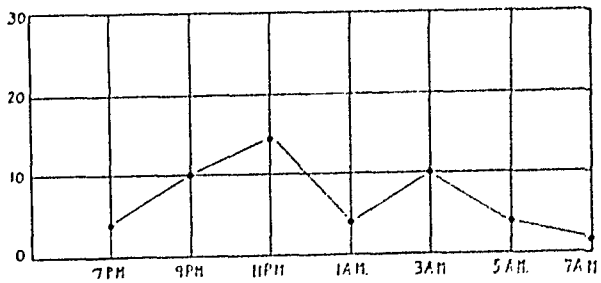


Fig. 4. Composite nocturnal curve of free hydrochloric acid in 14 gastric carcinomas.

cases were studied. The composite curve is given in Figure 5. In three cases there was marked hyperchlorhydria and, in two, a moderate increase in the acidity. The amount of secretion was high (140 c.c.). The peptic activity averaged 2.75 mm. It is interesting to note that, in two, the usual day fractional test meal revealed a very low curve as compared with the nocturnal curve.

Jejunal Ulcer After Partial Gastrectomy: Six cases were studied. The composite curve is given in Figure 6. Only two showed marked hyperchlorhydria. The amount of secretion was small (15 c.c.). Peptic activity was low (1.5 mm.).

The Effect of Partial Gastrectomy on the Night Secretion: This was studied in 21 patients with duodenal ulcer (Figure 7) and five patients with gastric ulcer (Figure 8). The marked reduction in acidity following partial gastrectomy is obvious. Fourteen of the 21 duodenal ulcer patients had a post-operative achlorhydria. The average quantities of secretion were reduced from 120 c.c. to 30 c.c. The Mett tube digestion preoperatively averaged 3.5 mm. and post-operatively 0.5 mm. The ferments were absent in all the achlorhydrias except one. Ten of these achlorhydrias were tested with histamine and neutral red. Of these, five were true and five false achlorhydrias. In the five patients with gastric ulcer, three had a true achlorhydria three weeks after the operation. The other two showed very little acid at that time and a few months later had a true achlorhydria. This gradual loss of the free hydrochloric acid after partial gastrectomy for

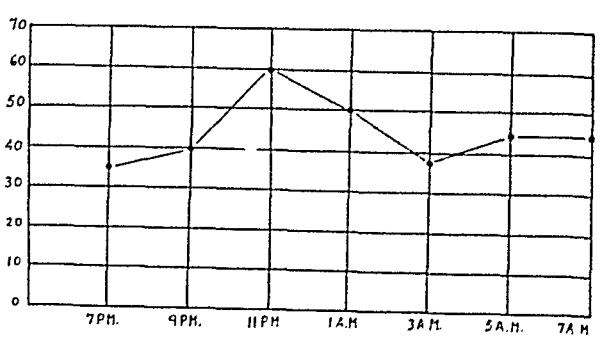


Fig. 5. Composite nocturnal curve of free hydrochloric acid in 5 gastro-jejunal ulcers after gastro-enterostomy.

ulcer is not uncommon in our experience. The ferments in the gastric ulcer cases showed 3.5 mm. Mett tube digestion before and zero after the operation.

Peptic Ulcer of the Esophagus: The opportunity of studying the night secretion occurred in one case. The curve was very high, reaching the figures of 119 at 11 P. M. and 118 at 7 A. M.

Gastric Neurosis: In three cases in whom ulcer was suspected but gastric neurosis finally diagnosed, the day fractional test meal revealed a marked hyperchlorhydria, whereas there was an achlorhydria during the night.

Attempts to Control the Night Secretion: I—In eight cases with duodenal ulcer a combination of a neutralizing agent (calcium carbonate and magnesium oxide) and two inhibitory substances (olive oil and atropine) were administered at 7 P. M. after aspirating the stomach as completely as possible. Accordingly 15 grains each of the alkali, two ounces of olive oil, and atropine sulphate, gr. 1 75, were given at 7 P. M. The results were as follows: (1) Two cases whose

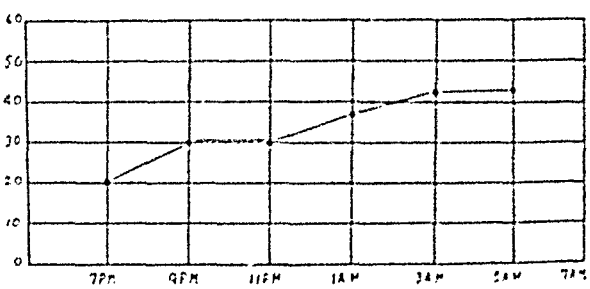


Fig. 6. Composite nocturnal curve of free hydrochloric acid in 6 jejunal ulcers after partial gastrectomy.

curves were moderate (20 to 40) were completely controlled throughout the night. (2) Two cases (curves from 20 to 50) were controlled for the first half of the night (to 1 A. M.). (3) In two cases (curves from 30 to 70) the curves were unaffected, and (4) in two other cases (curves from 20 to 60) the curves were higher than the controls. That is, in 75 per cent the free acid was not neutralized throughout the night by the combined effect of aspiration, neutralization and inhibition.

II—*The Milk Drip:* As mentioned in the introduction, the author has introduced a continuous milk drip (alkalinized with five grams of bicarbonate of soda to the quart) into the stomach through a fine calibred fractional Rehfuss tube, 30 drops per minute, throughout the day and night, as a treatment for gastric, duodenal and jejunal ulcer. (The chemical alkalinization of the milk is not strictly essential.) It is also useful for peptic ulcer of the esophagus, peptic esophagitis, cardiospasm, various types of malnutrition, hysterical nausea, vomiting and anorexia. The administration of various pharmacologic agents in this manner is being investigated. That the

milk drip does completely control the free acid is evidenced by the fact that numerous samples aspirated both during the day and night from many cases did not reveal any free hydrochloric acid. Also, it is interesting to note that after three weeks of the milk drip treatment, the acid curve tends to become considerably lower. Whether this is the result of the improvement in the ulcer or represents a new habit of secretion is difficult to answer. The change is portrayed in Figure 9 (reproduced from the author's article with the kind permisison of the Editor of the American Journal of the Medical Sciences).

COMMENT

The most striking findings in this study are:

1. The low or absent nocturnal free hydrochloric acid in normals.
2. The marked increase in the nocturnal secretion and acidity in ulcer patients (particularly duodenal ulcer).
3. The failure in most instances of pharmacologic methods to control the nocturnal acidity.

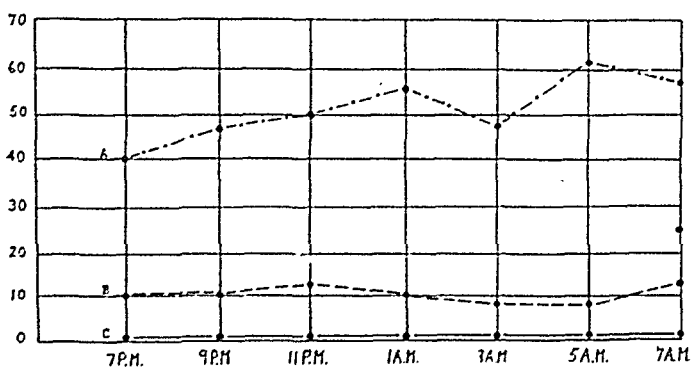


Fig. 7. Effect of partial gastrectomy on the nocturnal secretion in 21 duodenal ulcers.

4. The control of the nocturnal acidity by (a) the milk drip, and (b) partial gastrectomy.

Apparently, normal people in the absence of the normal food and psychic stimuli, do not secrete in response to the presence of the tube in the stomach. Whether the tube acts to inhibit secretion, cannot, of course, be answered.

In ulcer, particularly duodenal ulcer, the quantity and concentration of nocturnal free hydrochloric acid is very high. We have not made in these cases any exact studies of the time relationship of the well-known night pain in ulcer and the peak of gastric secretion. The finding of a high curve in the day test meal and a low one during the night in gastric neurosis may be helpful in the differential diagnosis. We have not encountered high curves in normals and only rarely low curves in duodenal ulcer.

Experimentally, free acid in the empty stomach seems injurious to the gastric mucosa, causing erosions and inflammation. Silbermann using oesophagotomized dogs and sham feedings, pro-

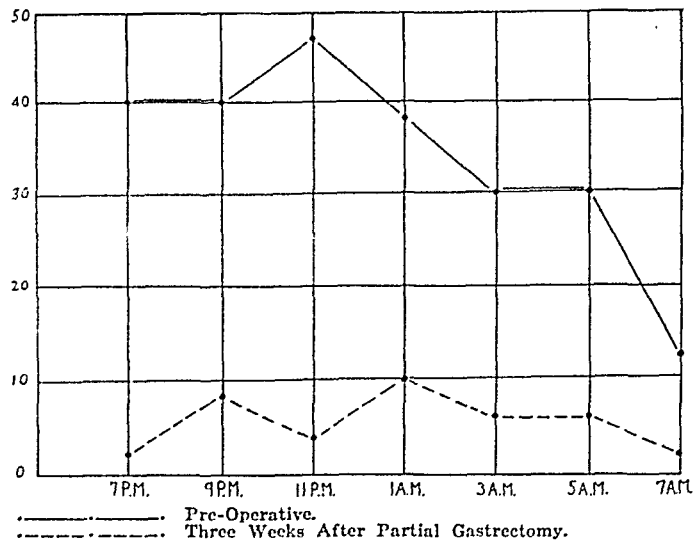


Fig. 8. Composite curve of nocturnal free hydrochloric acid in 5 gastric ulcers.

duced severe ulcerations in the gastric mucosa. Büchner (9) in Aschoff's laboratory, by a combination of histamine and starvation produced with regularity in 80 per cent, ulcerations in the "vormagen" of rats. Puhl (10, 11), who repeated these experiments, agrees that free acid in the empty stomach is injurious. Whether the hypersecretion and hyperchlorhydria during the night in ulcer is cause or result, it seems fair to suspect its harmful *rôle* in producing gastritis, duodenitis, irritating the ulcer, and probably producing night pains by its action on the ulcer bed (12).

In view of this experimental evidence, it seems highly desirable to neutralize the gastric secretion during the night. This, we believe, is most successfully accomplished in the milk drip treatment and constitutes the most potent argument for its use.

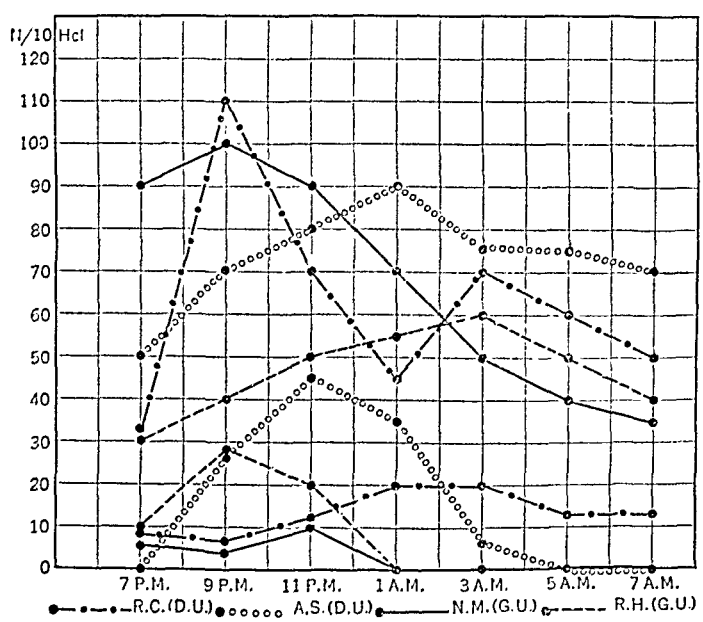


Fig. 9. The upper curves show the nocturnal free hydrochloric acid in 2 duodenal and 2 gastric ulcers. The lower curves show the night acidity after 3 weeks milk drip treatment.

It is important to note that the surgical procedure of partial gastrectomy for ulcer which has as its basis the reduction of the gastric acidity, not only reduces the acidity under the normal food stimuli in the waking state, but also during the night. In other words, when post-operative achlorhydria is present it is a real achlorhydria throughout the entire 24 hours. This is of great significance when one considers that in our experience we have not observed a recurrence in the presence of a post-operative achlorhydria.

We have not made a comparative study of cases of chronic gastritis or achlorhydria with reference to the day and night secretions. We believe that a true achlorhydria readily can be proved by using a histamine-neutral red-food combination in the usual day fractional test meal. It seems unnecessary to carry out night secretion studies in these cases.

Apparently by our studies no new light is thrown upon the secretory activities in gastric carcinoma and jejunal ulcer by the nocturnal studies.

In two recent papers (13, 14), Henning and Norpoth give their experiences with night, gastric secretion studies. They also found in a study of 91 cases, that normals (eight cases) did not have an acid secretion during the night, that ulcer patients had very high curves, and that histamine achylias also did not reveal free acid during the night. Their findings differ somewhat from ours in that they found no secretion during the night in seven of 41 cases of duodenal ulcer, and in five cases of gastric ulcer, and that seven cases of "vegetative neuroses" had a high curve during the night. Whether technical methods or difficulties in diagnosis account for the differences cannot be stated. In the main, however, their study and that here submitted agree; that is, that normals have a low nocturnal acid secretion and ulcers a high one.

SUMMARY AND CONCLUSIONS

1. The curve of gastric secretion during the night has been studied in 169 patients.
2. Normals have little or no free hydrochloric acid during the night.
3. Patients with duodenal, gastric, and jejunal ulcer have a high nocturnal curve and a high titre of free acid.
4. Gastric neuroses have a low nocturnal curve of secretion.
5. In gastric carcinoma, the gastric contents during the night resemble those found in the usual day test meal, i. e., a low acidity with increased mucus and blood.
6. The nocturnal hypersecretion and hyperchlorhydria in peptic ulcer cannot be controlled by alkalies, olive oil, atropine and aspiration.
7. In our opinion the best medical method of controlling the gastric secretion during the night is the milk drip. Surgically, partial gastrectomy frequently accomplishes the same result.
8. The significance of these findings particularly in the problem of peptic ulcer is discussed. Finally, the injurious effect on the gastric mucosa of an increased fasting or interdigestive secretion is emphasized.

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Clinical Notes Concerning Distal Ileitis as a Manifestation of Bacillary Dysentery

By

JOSEPH FELSEN, M.D.

NEW YORK CITY, NEW YORK

RECENT investigations have shown that bacillary dysentery, notably the Sonné-Duval and atypical Flexner types, may manifest itself clinically in many *bizarre* forms. Symptomless, constipated, meningitic and appendicular types of bacillary dysentery have been described (1-2). The present communication deals with distal ileitis which may be defined as "an acute inflammation of the terminal ileum, accompanied by mesenteric adenitis and caused by *B. dysenteriae*".

Submitted November 7, 1934.

CLINICAL FEATURES

The usual history is that of a dietary indiscretion, following which the patient complains of anorexia, lassitude and headache, sometimes accompanied by vomiting. Abdominal pain may not be a prominent feature for several days, but when

it occurs, there is definite localization to the right, lower quadrant. Also, there may be some localization in or near the *left*, lower quadrant. Tenderness generally is present, at or to the left of McBurney's point; it may be manifested on "rebound" and tends to shift with changing the position of the body. Spastic ileum and sigmoid occasionally are felt through a thin abdominal wall. Diarrhea is not a constant feature, but usually occurs at some time within the first week of the disease. The diarrhea may be profuse and constant or transient. It may be preceded, or succeeded, by constipation but, on the other hand, obstinate constipation may be present during the entire course of the disease. This appears strange in view of the commonly accepted understanding of typical bacillary dysentery. Repeatedly we have observed this phenomenon, however, in recent outbreaks of Sonné-Duval and atypical Flexner dysentery. This feature often is misleading, erroneously eliminating this infection from clinical consideration as a cause of a set of symptoms which usually are interpreted as indicating acute appendicitis. The pyrexia generally is quite moderate; there is a normal leucocyte count or even leucopenia early in the disease.

At operation, should it be performed, the appendix appears grossly to be normal, but the terminal ileum is reddened and its wall is distinctly thickened and edematous, giving the impression of primary, acute inflammation. The picture may be segmental, the redness and thickening stopping abruptly at a point approximately 30 cm. above the ileocecal valve. Beyond this the intestine appears to be healthy. The mesenteric vascular loops and arborizations are congested and the mesenteric nodes are enlarged, particularly on either side of the ileum and at the ileocecal angle. A clinical diagnosis of "mesenteric adenitis" usually is made, though such pathology simply is one manifestation of bacillary dysentery, just as terminal ileitis is another.

The post-operative course following appendectomy, which is the usual therapeutic procedure, is governed by the systemic effects of the bacillary dysentery. The disease, as encountered up to the present, runs a rather mild course with gradual subsidence of symptoms and pyrexia, and terminates in uncomplicated cases, in three to five weeks. Nothing as yet can be said with regard to the ultimate regression of the terminal ileitis. This is of particular interest in connection with the etiology of "idiopathic ulcerative colitis" and its extension to, or independent involvement of, the ileum.

It appears quite evident that some of these cases are instances of bacillary dysentery. Unless the feces are cultured early in the disease and repeated agglutination studies are made against typical and atypical dysentery strains, the diagnosis will not be proved. Our experience in the past three months is limited to five cases in three of which the clinical, operative, cultural and serological findings were those of atypical Flexner dysentery. The other two were of the Sonné-Duval type.* Only an adequate follow-up, which is now being carried out, will clarify the possible relationship between bacillary dysentery and idiopathic ulcerative colitis.

Since attention has been called to the appendicular form of bacillary dysentery, careful clinical and bacteriological study has eliminated operative interference in some cases. Certain of these patients had symptoms and signs suggestive of ileal involvement. All, including the cases mentioned above, apparently made complete recovery. If our interpretation of the pathology is the correct one, the lesion described represents the earliest stage in terminal ileitis inasmuch as infection preceded symptoms by only one or two weeks.

It is reasonably certain that, in some patients, the acute lesions may fail to heal, secondary nonspecific infection occurs, *B. dysenteriae* and the specific agglutination titre having disappeared. Within the limits of our recent experience, the sharply segmental nature of the lesions and general pathology speak for the common pathogenesis of terminal ileitis, idiopathic ulcerative colitis and bacillary dysentery.

*Two other cases with typical operative findings were studied too late after discharge from the hospital to secure corroborative agglutination, cultural and diagnostic phage tests.

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ABSTRACTS

DENIS, R.

Inflammatory Tumors of the Stomach. Arch. des Mal. de l'App. Digestif et des Mal. de la Diges., Octobre, 1934.

The greater number of gastrectomies performed during the last year under the impulse of Finsterer or Pauchet have led to a revision of our conceptions on many pathological conditions of the stomach. For instance, gastric ulcer seems to owe its periodicity more to the gastritis itself than to the ulceration. Of 60 gastrectomies done by the author, 20 of them diagnosed clinically as cancer included four inflammatory tumors, recognized as noncancerous by the microscopical pathology only.

Three observations are extensively presented, with their microscopical pictures. The first showed proliferating element of the plasmocyte type; the second, a tumor with homogeneous connective tissue of inflammatory origin

KRUSE, FRED H.

The Syndrome of Hypertonic and Atonic Colopathy. J. A. M. A., 103:1366 (November 3), 1934.

The term colitis should be limited to include only inflammatory states of the large bowel. The greater majority of chronic bowel disorders occur without any evidence of definite pathologic lesions of the mucous membrane.

The etiology of this group of cases has been assigned to either constitutional or functional factors or to local irritative lesions or general metabolic disorders. Although it must be admitted that adjacent inflammatory or irritative foci as, appendicitis or gall bladder and pelvic lesions may produce secondary bowel disorders, the results obtained in their treatment have been disappointing.

The study of the large bowel has led to the knowledge of different colon forms varying from the normal colon forms to redundancies and megacolon. Studies of motor function have demonstrated hypotonicity and hypertonicity in the colon leading to atonic constipation on the one hand and spastic constipation and mucous colitis on the other. In these conditions there is evidence of constitutional and functional disturbances of the autonomic nervous system.

The term "atonic constipation" is misleading because constipation due to uniform relaxation of the colon tube is rarely seen and possibly never exists throughout the whole length of the bowel at one time. Atonia is infrequent in the shorter bowel forms. It is found in the decompensated bowel segments of marked redundancies and in megacolon.

The main factors involved are the relative activity at various periods of the parasympathetic and sympathetic divisions of the autonomic nervous system. The parasympathetic, notably the vagus, is the activator, carrying fibers that increase secretion, produce spasticity and motor activity. If overstimulated, it leads to excessive formation of the mucus and to colic and hyperirritability. The sympathetic system is the inhibitor or depressor. Stimulation of this system leads to relaxation, loss of tone and to checking of secretion.

The "hypertonic colopathies" which include the spastic colon, the irritable colon, and mucous colitis, different phases of the same functional disorder, are not only local bowel derangements, but more apparently nervous and psychic disturbances.

In these cases, the following disturbance occurs: There is spasm in the descending and sigmoid colon, peristalsis and antiperistalsis in the cecum and adjacent bowel with prolonged stasis and excessive mucus secretion. As a class, individuals with functional colon disorders are more or less unstable. They are easily excited and worry a great deal. They are generally below par physically. Undernutrition and visceroptosis are common. About 75 per cent of these disorders occur in women.

The condition generally occurs in the second to the fifth decade. The constipation alternates with periods of diarrhoea. The stools are difficult to pass and they are negative for pus, parasites, and usually for blood. The diagnosis is made from the history and physical examination. Stools and sigmoidoscopic examination and gastro-intestinal X-ray studies are necessary, for the purpose of ruling out organic disease.

The stools show great variation in form, shape and consistency. They alternate with periods of small dry, marble-like masses followed by diarrhoea with great quantities of mucus.

In the treatment, rest, sedation, elimination of laxatives, and a bland and non-irritating diet are important.

Francis D. Murphy, Milwaukee, Wisconsin.

IVY AND SANDBLOM.

Biliary Dyskinesia. Ann. of Int. Med., XIII, 115 (August, 1934).

Under this intriguing title the authors unfold the historical development of the idea that disorders of motility may constitute a cause of biliary stasis and hence become a factor in gall bladder symptomatology without accompanying stone or inflammation.

The foundation for the present-day thesis was laid by Krukenburg in 1903; Aschoff and Bacmeister (1909) described "stasis gall bladder" found in the absence of inflammation or stone. This was linked to the clinical findings by Schmieden (1920) and the hypothesis advanced that some anatomical defect, such as a kink, constituted the hindrance. Berg (1922) advanced the thought that a functional disorder of the biliary passages might cause "biliary stasis". He found a hypertrophy of the muscle around the ampulla of Vater. Westphal carried the thought further and even ventured a classification of "biliary dyskinesia". He described the sphincter of Oddi as consisting of a muscle coat around the antrum and a second part surrounding the papilla; when the vagus nerve is stimulated below the diaphragm he thinks the gall bladder contracts and simultaneously the antral part of the sphincter exhibits peristaltic movement, while the papilla relaxes. Then, after visualizing these activities as physiological phenomena, he developed the conception that with yet greater stimulation of the vagus the antral sphincter is thrown into spasm, the gall bladder shows more powerful contractions and a painful spastic distention results. This is "hyperkinetic dyskinesia". Westphal thought he could further demonstrate that when the splanchnic nerve was stimulated the antral portion of the sphincter relaxed while the sphincter of the papilla contracted; this also permits of a distention of the gall bladder, but an atonic one, hence, little pain—a dull ache rather. This he called "atonic dyskinesia". Lyon, this year and in this Journal, merely renamed these two conditions when he used the terms "spastic dysfunction" and "atonic dysfunction". Smithies, 13 years before, referred to the condition as "physiological block". Newman (1933), however, while using the terms "spastic distention" and "atonic distention" questions the entity of these dyskinetic conditions.

With this historic background Ivy and Sandblom study the problem from two viewpoints: (a) Can the choledochoduodenal mechanism contract forcefully enough to keep the gall bladder from emptying under stimulation? (b) Can such a fruitless effort produce pain in an otherwise normal gall bladder? From results obtained on normal human subjects the authors conclude that *pain may be elicited from non-inflamed biliary passages by maximum pressure in their lumens when done quickly where a tonic musculature exists.*

In discussing the cause of the condition, the authors accept the common duct sphincter as a demonstrated site, but suggest that the duodenum and the structure at the juncture of the cystic duct and the gall bladder neck have possibilities. Further study is considered necessary to establish the existence of the "collum-cysticus sphincter". The actuality of "biliary dyskinesia" may explain a stasis which leads to infection and stone formation; it may establish the role of pregnancy in a cholelithiasis; it may offer a rational basis for gallstone colic without stones; it may explain the recurrence of symptoms after a cholecystectomy by visualizing an irritable or hypertrophied sphincter of the common duct.

Virgil E. Simpson, Louisville, Kentucky.

CANTAROW, A.

Noncalculous and Calculous Cholecystitis. Ann. Int. Med.; October, 1934; Vol. 4, pp. 540-551.

Cantarow reported previously that 70 of 234 patients with calculous and non-calculous cholecystitis showed hyperbilirubinemia or bromsulphalein retention or both. This present article is a continuation of his study in more detail in 512 cases; observations on the qualitative and quantitative van den Bergh reaction, bromsulphalein retention, plasma cholesterol concentration and urinary urobilinogen being made. The author does not state how the diagnoses were determined.

In the 49 cases of acute cholecystitis, 36 had essentially normal findings. Of the remaining 13, 8 showed at some

time hyperbilirubinemia; bromsulphalein retention was present in 11; hypercholesteremia in 2; hypocholesteremia in 4, and urobilinuria in 4. Of the 288 patients with chronic non-calculous cholecystitis, normal findings were present in 212. Retention of bromsulphalein *without* hyperbilirubinemia was found in 32 of the remaining 76. Hyperbilirubinemia and retention of dye were present in 29 and hyperbilirubinemia without dye retention in 15. Hypercholesteremia was noted in 4, hypocholesteremia in 15 and urobilinuria in 16.

Of the 138 cases of cholecystitis with calculi, but with the stones not present in the common duct, 61 showed altered findings. Retention of dye was present in 52, hyperbilirubinemia in 50, hypercholesteremia in 7, hypocholesteremia in 15 and urobilinuria in 15.

Thirty-seven patients with stone in the common duct were studied and 31 showed abnormal findings. Dye retention was present in 28, hyperbilirubinemia in 30, hypercholesteremia in 13, hypocholesteremia in 2 and urobilinuria in 7.

The author comments on the complicating factors necessarily present to produce jaundice in non-calculous cholecystitis and the findings and conceptions of other authors on this subject. The presence of bromsulphalein retention in 32 patients without hyperbilirubinemia the author feels indicates a dissociation of these two phases of the excretory function of the liver; and the rapid return of normal findings in many cases indicates functional rather than organic disease of the hepatic cells. Likewise hepatic functional impairment, the author believes, is not an uncommon complication of calculous cholecystitis in the absence of clinical jaundice or at times of hyperbilirubinemia. The author points out that the presence of stone in the common duct, is, of course, more likely to produce hyperbilirubinemia than stones elsewhere in the bile passages, 81 per cent of his 37 cases showing this. And although obstructive jaundice naturally limits the information that can be gained from the dye test, nevertheless, the capacity of the liver to eliminate bromsulphalein does not always parallel the decrease in bilirubinemia following spontaneous resumption of the flow of bile as was shown in 39 of the cases.

Cantarow emphasized 3 points obtained from this data which if borne in mind, he feels, should aid in diminishing the postoperative morbidity and mortality of operations on the biliary tract, namely: 1. That some evidence of disturbed hepatic function can be obtained in a fairly large proportion of cases of calculous and non-calculous cholecystitis; 2. That marked grades of retention of bromsulphalein may occur in patients with disease of the biliary tract in the absence of hyperbilirubinemia; 3. That in certain cases of stone in the common duct, some degree of retention of dye persists for a variable period after a previously high serum bilirubin concentration has returned to normal.

A. H. Aaron, Buffalo, New York.

GRANT, LUTHER F., AND SCHUBE, PURCELL G.

The Effect of Alpha Dinitrophenol (1-2-4) on Blood Cholesterol in Man. Jour. Lab. and Clin. Med.

The authors state in detail the physical properties and the actions of this highly potent metabolic stimulant and report investigations on its effect upon blood cholesterol in man.

Alpha dinitrophenol (1-2-4) is a crystalline solid with a melting point of 114 degrees centigrade, slightly soluble in water and more so in ether or alcohol. With half its weight of sodium bicarbonate a 3 per cent aqueos solution may be made.

The physiologic properties of alpha dinitrophenol can be enumerated as follows:

(1) Alpha dinitrophenol, when given to pigeons, rabbits, rats, cats, dogs and men, in doses ranging between 3 and 40 mg. per kilogram of body weight, by any route, produces a remarkable increase in body temperature, up to 6 or 7 degrees centigrade in conjunction with marked respiratory stimulation.

(2) The maximum febrile response occurs about one hour after injection or several hours after oral administration.

(3) The increased temperature can occur independently of the skeletal muscles or central nervous system.

(4) The temperature is not influenced by full doses of ergotamine, adrenalectomy or thyroidectomy.

(5) The respiratory stimulation may occur independently of the pyrexia.

(6) The pulse rate is increased.

(7) The blood pressure shows no consistent change.

(8) The nitrogen excretion is less than the nitrogen intake.

(9) The organic acid excretion is not increased.

(10) The weight is decreased.

(11) The metabolic rate is increased as much as from 25 to 50 per cent.

(12) Recovery, if the dose is not fatal, requires four or more hours.

(13) Death may occur as a result of direct circulatory depression, hyperpyrexia, acidosis or anoxemia, dependent on the dose, rate of injection, etc., or drug.

The effects upon the cholesterol metabolism are rather inconclusive and further studies are being conducted. To date, however, the effects in most cases seem to be an initial elevation of blood cholesterol, then a drop below the original level followed by a gradual return to normal. Doses of 5 grains a day by mouth were used for a period of 20 days with blood cholesterol estimations (Schoble method) before, during and after the test. Their observations on body weight during these experiments were opposed to other reports upon the effect of the drug. The largest definite weight loss was four pounds and this in only two of fourteen patients; three subjects actually gained five, twelve and seven pounds respectively. On the average there was little change in weight.

Further studies are promised to clear these inconsistencies.

B. B. Vincent Lyon, Philadelphia, Pennsylvania.

FARTHING, J. WATTS, AND BECK, JAMES S. P.

Urobilinuria False Ehrlich Reaction Caused by Pyridium Medication. Jour. Lab. and Clin. Med.

One of the authors observed an excessively high urobilinuria reaction in a patient taking pyridium and also that pyridium dissolved in water when tested with the acid solution of Ehrlich's reagent gave the characteristic red color of urobilin. A positive test was obtained with dilutions of 1 part in 75,000. Goerner and Haley had shown that a patient receiving .6 grams of pyridium by mouth daily would have a concentration in the urine of upward of 1 part in 3,000. The method of L. D. Scott of extracting with butyl alcohol is of no differential value because the dye from pyridium is also extracted with butyl alcohol. However, urines which were shown to contain urobilin by both Ehrlich's and Schlessinger's test when treated with HCl alone did not show the color change. It is, therefore, quite easy to detect this drug reaction by the addition of HCl. We have made it routine that all urines which come to our laboratory and are shown to contain urobilin by Ehrlich's test be tested for color changes on the addition of HCl alone.

This false reaction may be detected by treating all urines which are positive to Ehrlich's test with HCl alone. A pink or red color with acid indicates the presence of the dye. Discontinuing the pyridium for three or four days is apparently the only means of obtaining a true test for urobilin with the Ehrlich reagent.

B. B. Vincent Lyon, Philadelphia, Pennsylvania.

SECTION II—*Experimental Physiology*

The Inhibitory Effect of Histamine on Gastric Secretion*

By

ARMINE ALLEY, M.A.
MONTREAL, CANADA

IT WAS demonstrated by Babkin (1930), Vineberg and Babkin (1931), Gilman and Cowgill (1931) and Webster (1931) that, when gastric secretion was activated in the dog by a subcutaneous injection of histamine, the peptic power and the concentration of organic material in the gastric juice gradually decreased. Repeated administration of histamine produced a gastric juice in which the volume, total Cl concentration and acidity were not diminished in the least degree from values obtained after the first injection. But the digestive power and the concentration of organic material fell practically to zero in these circumstances.

The conclusion was drawn from these experiments that histamine stimulates only the parietal cells of the gastric glands without affecting the peptic and mucous cells. The fact that the peptic activity of the "histamine" gastric juice is somewhat higher at the beginning than at the peak of the secretion was explained as due to the "washing out" of zymogenous material, presumably accumulated in the tubules of the glands during inactivity or possibly lying loosely at the apices of the peptic cells. However, this explanation of the mode of stimulation of the gastric glands by histamine did not seem adequate to cover all the facts noted in the corresponding experiments. It was especially difficult to explain the effect of repeated administration of histamine since the gastric mucosa secreted in these circumstances an acid solution practically free from other substances. The possibility occurred to us that histamine may have a two-fold effect on the gastric glands, selectively stimulating the parietal cells and inhibiting the activity of the peptic and mucous cells. It was with the aim of testing this latter supposition experimentally that the present work was undertaken.

METHODS

Subcutaneous injection of histamine hydrochloride was given to dogs previous to sham-feeding or ingestion of milk or meat and during secretion on sham-fed milk or meat. In the first type of experiment the sham-feeding was not started until fifteen minutes after the histamine secretion had stopped. The dogs were sham-fed with raw minced beef-heart or milk for five minutes. Four dogs were used, two with both oesophagotomy and a gastric fistula (dogs "K" and "R") and two with innervated gastric pouches, one from the lesser curvature region (Armour (1930) pouch, dog "W") and the other from the greater curvature region of the stomach (Pavlov pouch, dog "B"). The fluid volumes, the pepsin as determined by Nirenstein and Schiff's modification of Mett's method (Hawk and Bergeim (1927)) and the total and free acidities as determined by phenolphthalein and Töpfer's reagent respectively, were recorded. The experiments were started when the secretory activity of the gastric mucosa was minimal, *i. e.*, when approximately 0.3 c.c. of acid mucoid fluid per fifteen minutes was produced by the pouch or 3 c.c. per fifteen minutes from the whole stomach.

EXPERIMENTAL RESULTS

Figures 1 and 2 and Table I demonstrate the inhibitory effect which a previous injection of his-

TABLE I

Gastric secretion from the whole stomach on milk or on meat sham-fed to dog "K" for five minutes with and without a previous histamine injection.

Procedure	Vol. c.c. per ¼ hr.	Acidity Total m. eq./l.	Acidity Free m. eq./l.	Peptic Power	Procedure	Vol. c.c. per ¼ hr.	Acidity Total m. eq./l.	Acidity Free m. eq./l.	Peptic Power
Exp. April 30					*Exp. April 8*				
Milk sham-fed	30	140	102	200	Meat sham-fed	60	153	104	196
	15	144	103	182		46	153	106	196
	13	142	106	202		39	149	108	305
	14	144	108	225		26	144	98	154
	15	143	104	144		14	146	90	196
	10	141	100	144		12	144	94	256
	3	136	95	180		5	140	96	305
Total	100	...	...	19446	Total	202	...	...	54016
Average	...	141	103	194	Average	...	149	101	267
Exp. April 23					*Exp. March 26*				
Histamine (0.9 mg.)	25	136	102	144	Histamine (0.9 mg.)	62	145	98	77
	47	148	114	9		52	160	113	16
	54	148	116	4		39	159	112	16
	37	153	125	9		4	149	106	4
	16	150	120	16					
	2	110	78	36					
Total	181	...	...	...	Total	157	...	...	...
Milk sham-fed	13	140	102	248	Meat sham-fed	9	117	76	282
	17	149	108	243		14	136	96	324
	7	141	101	370		13	146	100	225
	4	134	94	429		11	146	101	305
						5	141	98	313
						1	138	95	384
Total	41	...	...	11561	Total	53	...	...	15895
Average	...	143	103	281	Average	...	138	95	289

*Department of Physiology, McGill University.
Submitted November 7, 1934.

Fig. 2. Dog "K". Inhibition by histamine of gastric secretion stimulated by sham-feeding with meat.

TABLE IV

Effect of previous pilocarpine secretion on the secretion produced by sham-feeding with milk in dogs "K" and "R". (The juice was always contaminated with bile in dog "R".)

Dog	Date	Pilocarpine Secretion				Sham-feeding Secretion			
		Vol.	Acidity		Peptic Power	Vol.	Acidity		Peptic Power
			Total	Free			Total	Free	
		c.c.	m. eq./l.			c.c.	m. eq./l.		
"K"	May 16	83	129	90	299	110	142	101	144
"R"	Mar. 9	75	98	45	156	101	140	93	291

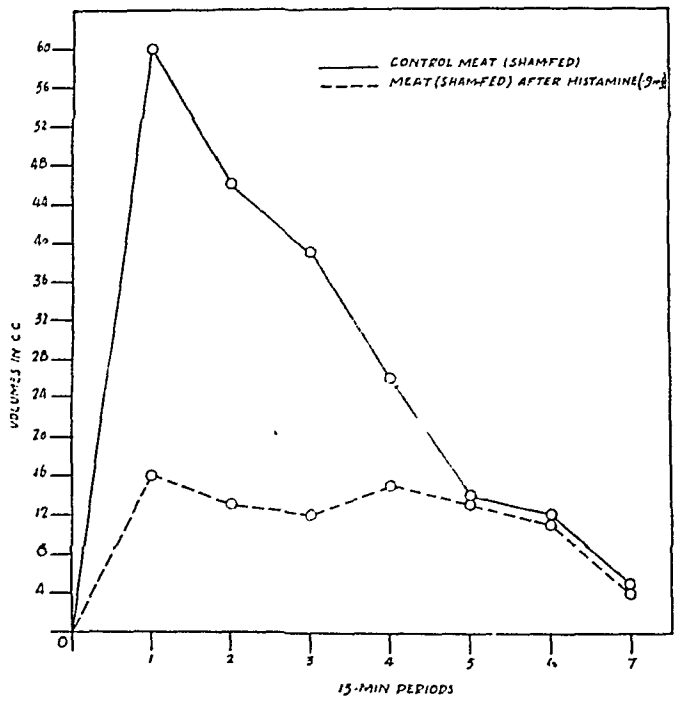
In another type of control experiment, a dog with oesophagotomy and a gastric fistula ("K") received two successive injections of histamine, the second injection being given immediately after the cessation of the secretion from the first injection. The effect of the second histamine injection was not only not inhibited but was somewhat increased, as can be seen from Table V. With the increased flow of juice, both total and free acidities were somewhat increased. The same is true about the peptic power of the juice. Therefore, the inhibitory effect of histamine on the subsequent secretion activated by sham-feeding is a characteristic feature of the effect of this drug. It is due neither to the loss of body fluid nor to the "fatigue" of the gastric glands.

The above experiments were repeated on two gastric-pouch dogs. In these experiments also, histamine had an inhibitory effect on the subsequent secretion obtained by ingestion of milk and meat, as may be seen in Figures 4 and 5 in the case of dog "B" (Pavlov pouch). The secretion on meat was less affected than that on milk. A probable explanation of this difference is that in

TABLE V

Gastric secretion from the whole stomach of dog "K" on two histamine injections, the second injection given on cessation of the secretion from the first.

Procedure	Vol.	Acidity		Peptic Power	Pepsin Output
		Total	Free		
	c.c. per hr.	m. eq./l.			
Histamine (0.75 mg.)	16	120	84	64	1024
	35	144	116	16	560
	27	148	116	9	243
	14	144	114	16	224
	19	139	112	20	380
	4	132	108	77	308
Total	115	...	...	...	2739
Average	...	138	108	34	
Histamine (0.75 mg.)	15	133	104	144	2160
	54	148	123	16	864
	50	150	120	16	800
	26	152	122	48	1248
	2	139	100	64	128
Total	147	...	...	...	6300
Average	...	144	114	58	



the case of milk, a summation of the inhibitory influences of histamine and fat occurred. On meat, the most noticeable inhibitory effect occurred during the first fifteen minutes of the secretion. Similar results were obtained on dog "W" (Armour pouch).

In Table VI data are presented on the effect of preliminary stimulation of the gastric glands with histamine and the subsequent feeding with milk or meat in Pavlov-pouch dog ("B") and Armour-pouch dog ("W"). When food was given fifteen minutes after the end of the histamine secretion, the volumes of the secretions were diminished, and the acidities were somewhat lower, probably in connection with the diminished rate of secretion. The results in pepsin show some variation, the peptic power and output being lower than normal in dog "B" and higher than normal in dog "W" in the sham-feeding secretion after histamine.

Control experiments with a preliminary pilocarpine administration as well as with repeated injections of histamine were also performed on the pouch dogs. There was no inhibition of the post-prandial secretion or of the effect of the second injection of histamine, as can be seen from the following data.

Curves of the volumes of the secretion on milk which was fed to the pouch dog "B", with and without previous pilocarpine injection, are seen in Figure 6. The volumes were not inhibited by this drug but rather increased. The total volume (27.0), average total and free acidities (139 and 92 respectively), and peptic power (63) did not vary greatly from those of the normal secretion on milk (see Table VI). The previous injection of 4 mg. of pilocarpine produced a volume of 24.7 c.c. with average total and free acidities of 131 and 73 respectively and an average peptic power of 599.

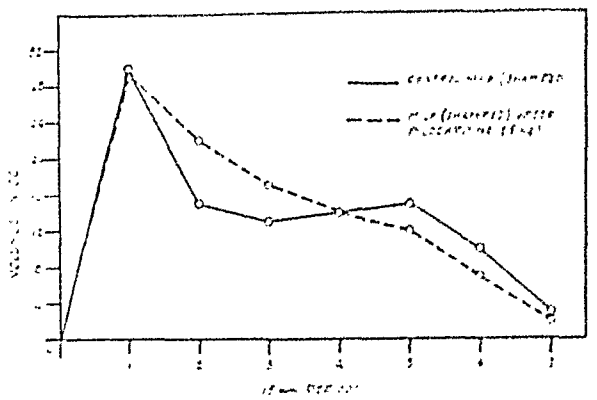


Fig. 3. Dog "K". No inhibition of gastric secretion stimulated by sham-feeding with milk after pilocarpine injection.

Two histamine injections were given to dog "B", the second injection following immediately on the cessation of the secretion from the first (Figure 7). The two curves are almost identical. In Table VII it will be seen that the figures for acidities, peptic powers and outputs were fairly close.

The inhibitory effect of histamine on the secretion on butter was seen in another type of experiment on the Pavlov-pouch dog "B". Histamine was injected at the beginning of the fourth hour of the secretion on butter. Immediately after the injection there was a complete inhibition of gastric secretion for eight minutes, after which a secretion typical for histamine occurred which was slightly low in volume but otherwise normal. On cessation of this secretion there followed an almost complete inhibition of the butter secretion with a very small flow at the end of the sixth hour.

A further type of experiment was carried out on the oesophagotomy dog "K", in which histamine was injected during the sham-feeding secretion on milk and meat. A most striking effect was seen on the peptic power in that it fell to the histamine level. On giving the usual injection of 0.9 mg. of histamine during the sham-feeding, there was not only no inhibition of the volume of the sham-feeding secretion but the total volume added up to more than the two control secretions together (meat 197 c.c., histamine 149 c.c. and meat plus histamine 449 c.c.). Thus there was a great dilution of the sham-feeding juice with the juice stimulated by histamine, which would cause a lowering of the peptic power. To avoid the dilution factor and restrict the effect of histamine on the volume of the secretion in the experiments illustrated by Figures 8 and 9 and Table VIII, smaller amounts of histamine, 0.7 mg. to 0.5 mg., were injected during the secretion provoked by sham-feeding. In these experiments extremely low peptic powers were also obtained. If these peptic powers be multiplied by the respective fluid volumes (output of pepsin), it will be seen (Table VIII) that the figures approach those of the peptic output in the secretion on histamine (Exp. May 30.) It would be expected that if the sham-feeding stimulus were producing juice with its usual high peptic power, the admixture of the above histamine juice would never decrease the peptic power to such a degree.

Therefore, the effect of histamine, superimposed on gastric secretion activated through the parasympathetic nervous system, definitely inhibited the discharge of the enzymes from the peptic cells but did not interfere with the secretory work of the parietal cells.

The inhibitory effect of histamine appeared immediately on injection, causing both the peptic power and output of pepsin to fall progressively. This was followed by a rise back to the sham-feeding level again, in the case of the peptic power but not of the peptic output. On the administration of larger doses of histamine (0.9 mg.) the peptic power did not return to the sham-feeding level but remained quite low. Also, with doses of 0.9 mg. of histamine the acidity was increased to a histamine level (total, 159, and free, 120 m.

TABLE VI

Average totals for gastric secretion obtained on feeding of milk and of meat to dogs "B" and "B'", with and without a previous histamine injection.

TABLE VII

Gastric secretion of Pavlov-pouch dog "B" on two histamine injections, the second injection given on cessation of the secretion from the first.

Fig. 4. Dog "B", with a Pavlov pouch. Inhibition of gastric secretion on ingestion of milk after secretion produced by histamine.

TABLE VIII

Gastric secretion from the whole stomach of oesophagotomy dog "K" on sham-feeding of meat and milk, on injection of histamine during meat or milk sham-feeding, and on injection of 0.5 mg. of histamine alone.

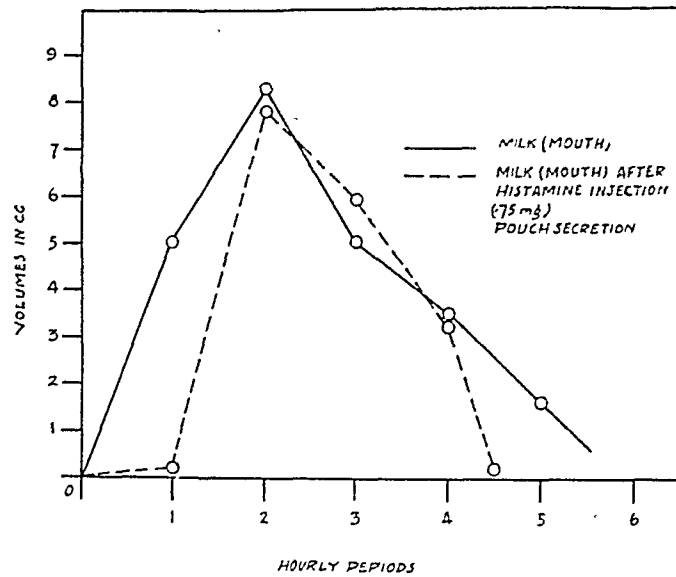
Procedure	Vol.	Acidity		Peptic Power	Pepsin Output
		Total	Free		
	c.c. per ¼ hr.	m. eq./l.			
Exp. March 23					
Meat	46	145	102	144	6624
	38	150	108	196	7448
	35	154	117	202	7070
	23	150	108	225	5175
	22	144	110	243	5346
	14	138	100	256	3584
	6	128	92	225	1350
Total	184	...	...	...	36597
Average	...	144	105	213	
Exp. April 30					
Milk	30	140	102	200	6000
	15	144	103	182	2730
	13	142	106	202	2626
	14	144	108	225	3150
	15	143	104	144	2160
	10	141	100	144	1440
	3	136	95	180	510
Total	100	...	...	...	18640
Average	...	141	103	194	
Exp. May 30					
Histamine	12	140	98	117	1404
(0.5 mg.)	25	153	114	36	900
	19	151	110	7	133
	11	148	112	9	99
	4	145	105	16	64
	1	138	100	42	42
Total	70	...	...	...	2642
Average	...	145	106	37	
Exp. April 18					
Meat	41	148	114	164	6724
Histamine	39	152	118	64	2496
(0.5 mg.)	70	158	127	4	280
	55	155	123	16	880
	49	157	118	25	1225
	28	152	120	56	1568
	6	139	104	144	864
	1	133	88	282	282
Total	229	...	...	...	14319
Average	...	149	114	94	
Exp. May 11					
Milk	15	119	88	144	2160
Histamine	23	138	104	64	1372
(0.5 mg.)	50	148	108	30	1500
	33	148	110	11	363
	22	148	105	25	350
	13	148	100	70	910
	5	144	100	196	980
Total	161	...	...	...	7635
Average	...	141	102	77	

eq./l). This was not seen when 0.5 mg. of histamine was injected during secretion activated by sham-feeding with milk.

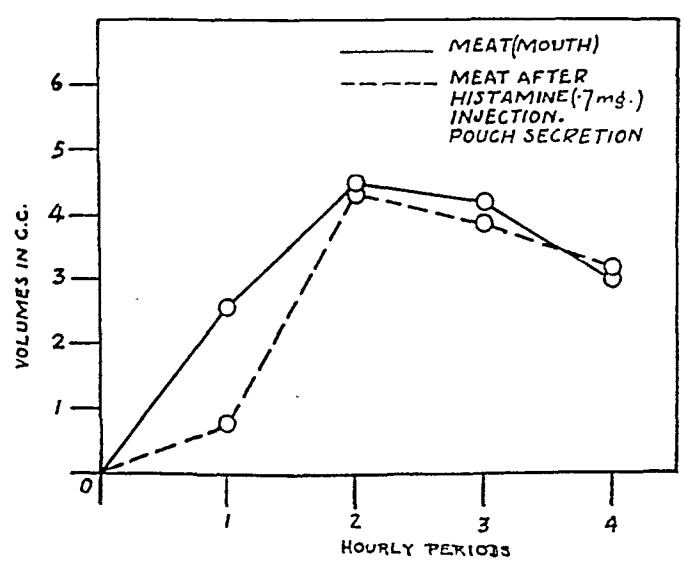
DISCUSSION

This investigation establishes a new property of histamine as an agent acting on the gastric mucosa. This substance not only stimulates gastric secretion but, in certain circumstances, inhibits it.

Fig. 5. Dog "B". Same as figure 4 except that the dog was fed with meat.



When Babkin (1930) and Vineberg and Babkin (1931) established the fact that gastric juice, stimulated to flow in the dog by subcutaneous injection and especially by repeated injections of histamine, is extremely poor in organic substances and pepsin, they advanced the theory that histamine stimulates the parietal cells only. The relatively high proportion of pepsin in the first samples of the juice was believed by them to be due to the "washing out", by a sudden flow of gastric juice, of the zymogen granules from the glandular tubules, where they had accumulated owing to continuous formation and slow discharge from the peptic cells. However, the relations as shown by this investigation would seem to be more complicated. Certain facts suggest that histamine, in addition to stimulating the parietal cells, prevents the discharge of the zymogen and mucus granules from the peptic and mucoid cells. This is evident from the extremely rapid fall of the peptic power of the juice and its organic moiety during the secretion activated by histamine. But after the end of such secretion, another stimulus (sham-feeding or food), which is able to activate



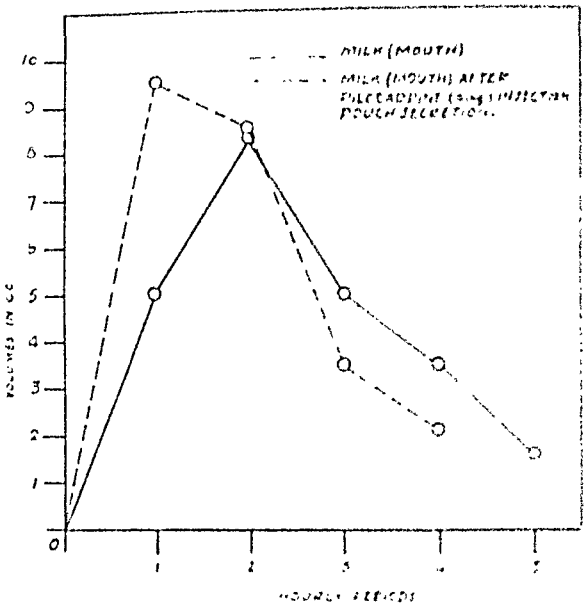


Fig. 6. Dog "B". No inhibition of gastric secretion stimulated by a meal of milk after secretion produced by pilocarpine.

the peptic and mucoid cells, produces in most cases a gastric juice with a higher peptic power than in control experiments where there was no preliminary administration of histamine. It would seem that during the action of histamine on the gastric mucosa there occurs an accumulation of zymogen granules in the peptic cells so that afterwards they are discharged in a greater number than usual.

Especially interesting facts were revealed in the experiments in which the gastric secretion stimulated by histamine was followed by one induced by sham-feeding or ingestion of food. In both cases there was a marked inhibition of the volume of the secretion. This inhibition was extremely pronounced in the case of sham-feeding and lasted through almost all the secretory period. When food was ingested by an animal with a gastric pouch in the usual manner and remained in the stomach, the inhibition was noted chiefly at the beginning of the secretion. Since, in sham-feeding experiments, the impulses to the gastric glands are conveyed through the vagi, it is obvious that a preliminary administration of histamine inhibits the secretory effect of the parasympathetic nervous system on the gastric glands. The same explanation could be applied to the inhibition of the initial phase of gastric secretion after ingestion of food because it is due chiefly to a reflex action transmitted to the gastric glands along the vagi. The chemical phase of gastric secretion did not seem to be affected essentially by previous histamine injection. It is a remarkable fact that the histamine inhibition of the volume of the gastric secretion occurs only when histamine is administered *before* the vagi are brought into activity. If histamine was injected during the vagal secretion, e. g., induced by sham-feeding (Table VIII), not only was the secretion not diminished but there occurred a summation of the two stimuli. Nevertheless, the secretion of pepsin undoubtedly was inhibited to the greater degree. In other words, the activity of the parietal cells, initiated by the vagi, was not inhibited by histamine, whereas, the activity of the peptic cells was inhibited. Using the old terms "secretory" and "trophic" as applied to functions of the nerves, we may say that histamine had not affected the "secretory", but only the "trophic" function of the vagi. But when histamine secretion occurred before the parasympathetic nervous system was brought into activity, the "secretory" effect of the vagi, as we have seen above, was also markedly diminished.

In connection with these findings it is worth while to remember the data of Browne and Vineberg (1932). These authors demonstrated that the state of rest or activity of the gastric glands determines, in many instances, their response to certain influences. Thus the hyperventilation of the animal had little inhibitory effect when histamine gastric secretion was established in contradistinction to vagal secretion. On the other hand, no secretion was obtained under histamine stimu-

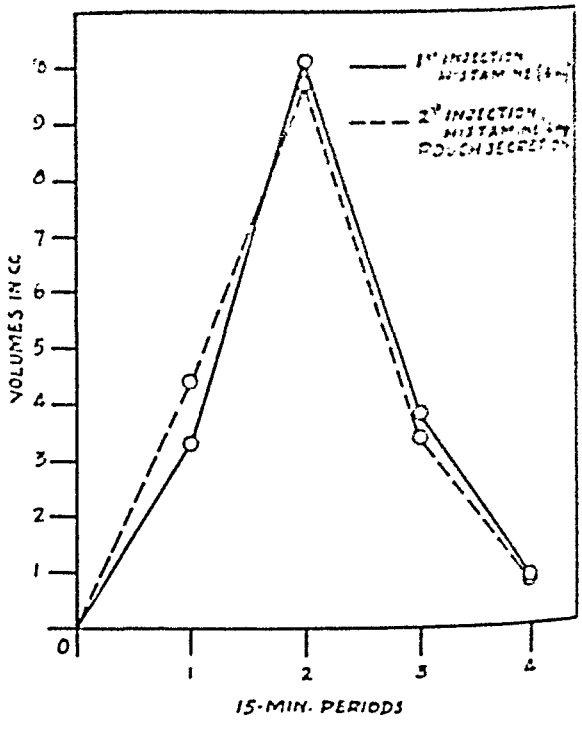
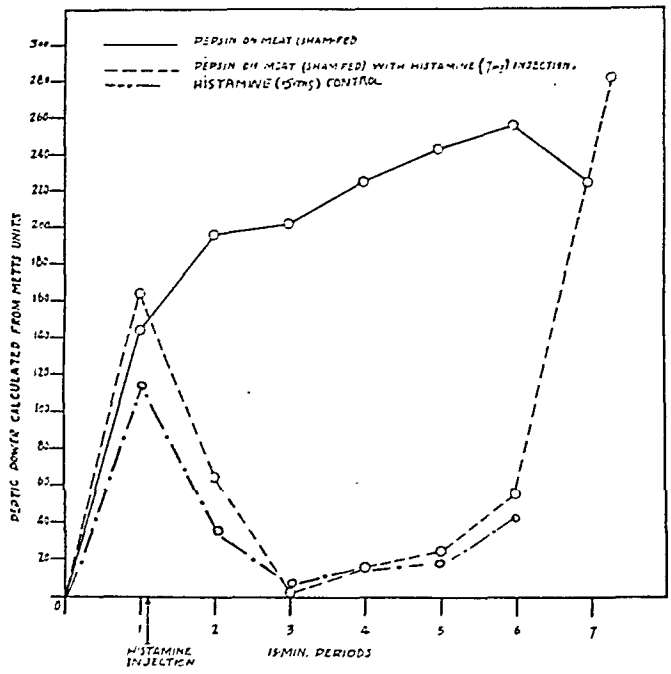


Fig. 7. Dog "B". Previous histamine secretion does not inhibit gastric secretion provoked by a second administration of histamine.

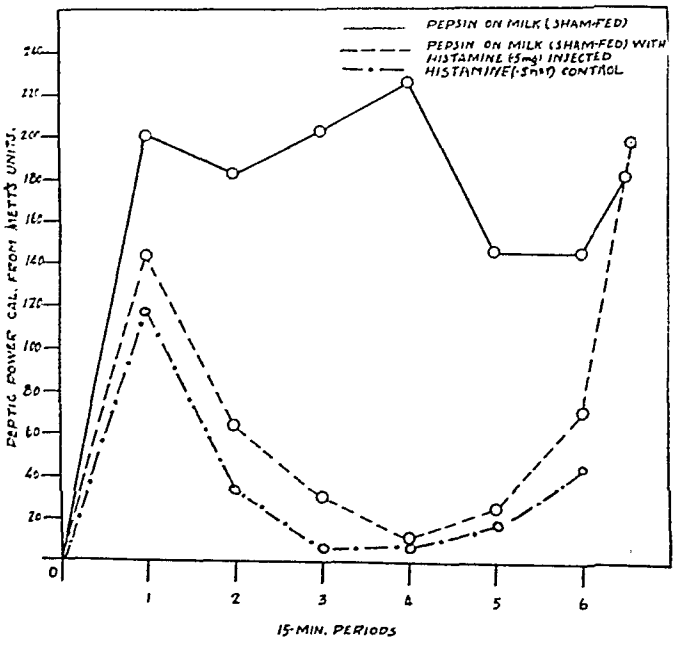
Fig. 9. Dog "K". Same as figure 8 except that the dog was sham-fed with meat.



lation in several cases of initial acidosis with low CO_2 and pH. But when acidosis was produced by the administration of acid during histamine secretion, no inhibitory effect was noted.

The conclusion that may be drawn from the experiments carried out during this investigation is that histamine stimulates only the parietal cells and inhibits the activity of the peptic and mucoid cells of the gastric glands. This fact emphasizes once more the validity of the contention put forward by our laboratory that in compound glands, such as gastric glands, various groups of secretory epithelia are regulated by different nerves or hormones. This does not exclude, of course, the co-ordination of the secretory work of these epithelial groups or the reactivity of one and the same group to different impulses, as is the case, for example, with the parietal cells in vagal or histamine secretion.

One more point must be introduced. It is believed by some clinical investigators (see *e. g.*, Bloomfield and Polland (1933)) that histamine is an adequate stimulus for the secretion of both acid and pepsin. It is very doubtful if the regulation of the work of the gastric glands in man differs so fundamentally from that observed in the dog or cat. The reaction of the gastric glands to histamine in man probably is of the same type as in experimental animals. The conclusion that histamine stimulates the peptic cells was drawn from experiments on man in which much smaller doses of histamine (0.1 mg. per 10 kgm. of body weight (Bloomfield and Polland, 1933, p. 77; 0.6 mg. per patient (Polland, 1932)) were employed than are usually applied to experimental animals (about 0.35 to 0.5 mg. per 10 kgm. of body weight). Therefore, the true nature of the action of histamine on the gastric glands could not be revealed.



SUMMARY

1. Subcutaneous injection of histamine not only activates but, in certain circumstances, inhibits gastric secretion in the dog.

2. Sham-feeding in a dog with oesophagotomy and a gastric fistula, or ingestion of food by a gastric-pouch dog, produces a smaller secretion of gastric juice with a higher peptic power, when applied after the cessation of the secretion provoked by histamine.

3. If histamine is administered during secretion stimulated by sham-feeding, the volume of the gastric juice secreted increases but the peptic power falls almost to the level of that of the secretion on histamine alone.

4. The explanation is advanced that histamine, while stimulating the parietal cells, inhibits the action of the vagi on the peptic cells, preventing the discharge by them of zymogen granules.

ACKNOWLEDGMENT

The writer is greatly indebted to Dr. B. P. Babkin for the suggestion of this problem and for the advice and criticism given; also to the Banting Research Foundation for providing a grant to carry on this work.

Fig. 8. Dog "K". Histamine injected during secretion activated by sham-feeding with milk. Note the sharp fall in the peptic power of the juice.

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ABSTRACTS

OLMER, J., ET BENBEKASSA, R.

Investigation into Insufficiency of the External Secretion of the Pancreas in the Presence of Chronic Cholecystitis and Infectious Hepatitis. Arch. de Med. gen. et coloniale, Tome 3, No. 2, 1934.

The authors have investigated into the lipolytic value on olive oil of the pancreatic secretions stimulated by the injection of 60 c.c. of milk by the duodenal tube or by the intravenous injection of secretin, after the Meltzer-Lyon method. The lipasic power is calculated according to the amount of cubic centimeters of sodium necessary to neutralize the acidity of the digestive juice, which normally varies between 70 and 80 units tenth-normal of sodium.

A marked diminution in the activity of the ferments is constantly encountered in chronic cholecystitis. After a cholecystectomy the lipasic power comes back to normal.

Recent research has considered the pancreas responsible to a certain extent for infectious hepatitis ("ictère catarrhaux"). As a matter of fact the lipasic power in the authors' research, varies between 90 and 120 units in the pancreatic juice after an injection of milk or secretin. Only two patients were eliminated from the statistics, as having a decreased lipasic power, because they showed a positive Wassermann. The contradictory results can only be explained by an inconsistent mechanism, different according to the cases.

If a pancreatic factor often is met with in infectious hepatitis, at any rate this factor is far from being a constant factor in determining that hepatitis.

Jean R. A. Le Sage, Montreal, Canada.

FARTHING, J. WATTS, AND BECK, JAMES S. P.

Urobilinuria—False Ehrlich Reaction Caused By Pyridium Medication. J. Lab. and Clin. Med. 20:61, 62, October, 1934.

The authors report a case of false bilirubin reaction with Ehrlich's reagent in a patient taking pyridium by mouth and as a result of several methods employed, state that there is no true test for urobilin with Ehrlich's solution in any case taking pyridium, except after discontinuance of the drug for three or four days. Schlesinger's test for urobilin, however, does not give a positive reaction with pyridium excreted in the urine.

M. G. Vorhaus, New York, New York.

IVY, A. C., AND BERGH, G. S.

The Applied Physiology of the Extrahepatic Biliary Tract. J.A.M.A., 103:1500, November 17, 1934.

The gall bladder manifests three types of activity; namely, absorption, secretion and motor activity.

In the process of absorption, the gall bladder concentrates the liver bile from four to ten times. The gall bladder is capable of storing a concentrated, entire, twelve or twenty-four hour output of liver bile. The bile ducts of animals possessing gall bladders do not concentrate to

[illegible] the sphincter of Oddi [illegible] matters whether the gall bladder will evacuate when the sphincter is spastic, biliary colic may be produced by causing the gall bladder to contract.

Present day evidence supports the theory that when the gall bladder contracts, the sphincter relaxes and when the sphincter contracts, the gall bladder fills. Whether this is due to a reciprocal nervous mechanism or is only passive, is not settled. The authors state that on weighing the evidence pertaining to the relationship between the gall bladder and the sphincter of Oddi, they are convinced that the gall bladder and the sphincter constitute a functional unit.

Prevention of gall bladder disease may be aided by the daily evacuation of the viscus by the appropriate intake of fat. This applies particularly to the gall bladder which evacuates slowly and incompletely.

In acute biliary disease not demanding an immediate operation, sedation should be employed. Foods, as fatty meats, and acid fruit juices should be withheld. Magnesium sulphate can be used with benefit.

In cases of chronic cholecystitis, with or without stones, excitant foods must be reduced to meet the patient's tolerance. The "tolerance" can only be determined after dietary experimentation.

The evidence today as regards cholecystectomy is strongly presumptive that the gall bladder is not benefited by drainage because if the mucosa is not permanently damaged, the scarring incident to drainage may interfere with normal emptying.

Cholecystectomy is indicated in patients with multiple small stones and where the gall bladder is non-functioning. Cholecystoduodenostomy or cholecystogastrostomy with or without gastroenterostomy leads, in the course of several months, to an ascending biliary tract infection and hepatitis.

The evidence today is inadequate to warrant the statement that actual damage is done to the patient by removing a gall bladder which functions. The fact that physiologic and anatomic changes do result following the removal should cause the surgeon to be hesitant about the removal of such a gall bladder until medical treatment has been tried.

Francis D. Murphy, Milwaukee, Wisconsin.

SECTION III *Nutrition*

Vitamin "A" as a Prophylactic Against the Common "Cold" in Groups of School Children

By

ESTHER M. TRESS, M.A., (Columbia)*
LONG BEACH, NEW YORK

INASMUCH as the common "cold" is the major cause of absences in the Long Beach Schools, for several years we have attempted to solve the problem in various ways. We have checked ventilation, adequate and suitable clothing, treated defects of tonsils, adenoids and abscessed teeth, have instituted exclusion from school of those suffering from colds, etc., but have been unable to note any appreciable improvement in the resistance of the children to the common cold.

Recent research indicates that a lack of Vitamin A in the diet decreases the resistance of the body to various types of infection, including infections of the respiratory tract (1).

In view of this recognized anti-infective property of Vitamin A, we became interested in observing whether or no the absences of pupils from school on account of colds could not be reduced if the children's diets were supplemented with cod or haliver oil.

MATERIAL STUDIED

In the Fall of 1932, we began a Vitamin A demonstration. We recommended that all children, especially those who had been affected with colds the previous year, take cod or halibut liver oil from October to March. For those who had difficulty in taking these fish oils at home, we proposed to give at the school one haliver oil capsule (plain) every school day at cost. Two hundred fifty three children (5-12 years of age) took haliver oil capsules at school and many more took these or cod liver oil at home. As a means of control we selected a comparable group but, in a short time, many of the controls began to take haliver oil so that this group of controls had to be abandoned.

*Supervisor of Health Teaching in the Long Beach, New York Schools.

Submitted November 5, 1934.

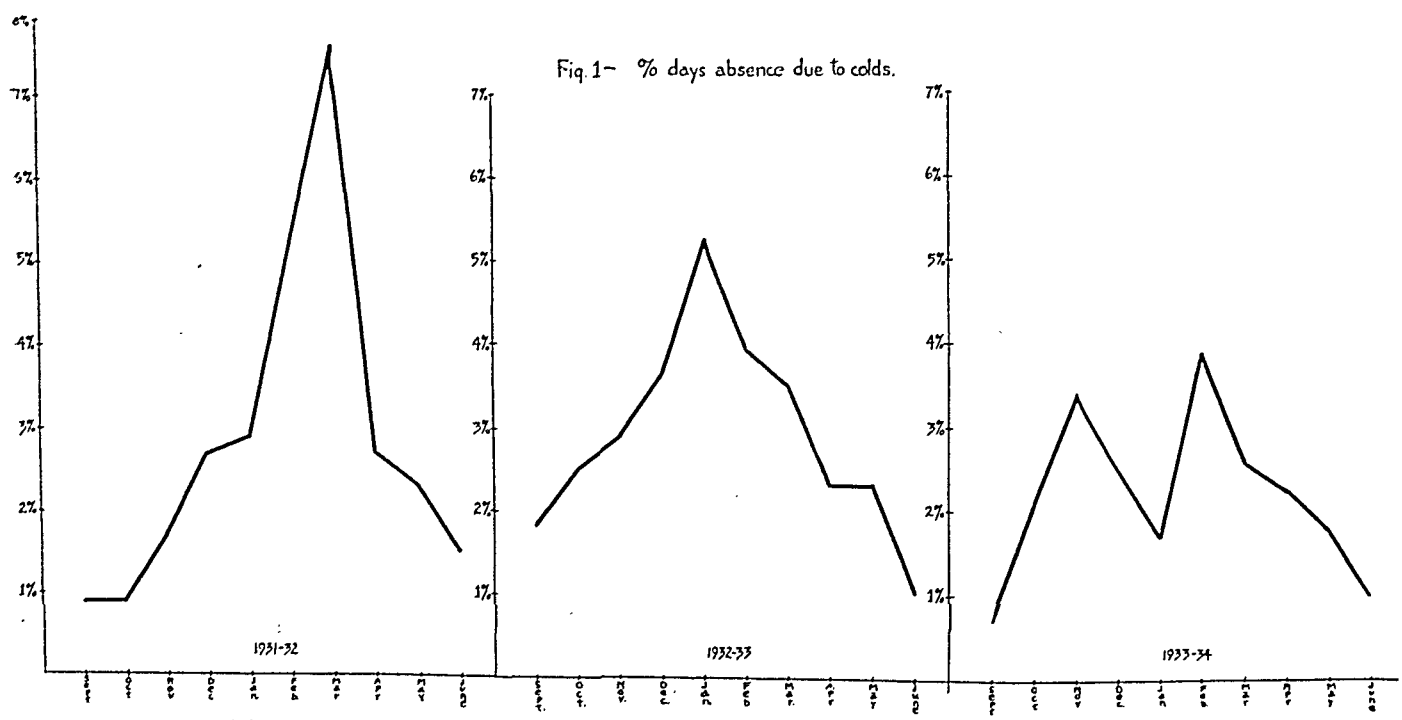


Fig. 1. Graph showing per cent days absence due to colds for three consecutive years.

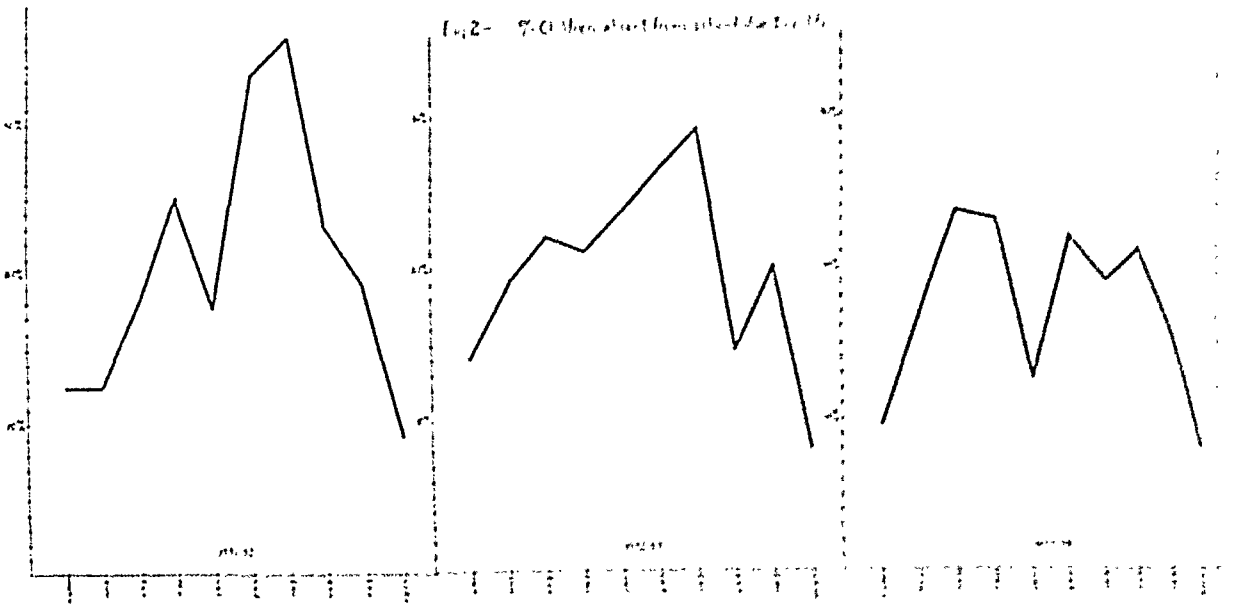


Fig. 2. Graph showing per cent children absent with colds for three consecutive years.

DATA OBTAINED FROM PROCEDURES ADOPTED

In evaluating the results of our first year's work we checked observations from two angles: (a) school attendance reports; (b) parents' reactions based upon responses to a questionnaire.

TABULATION I

(a) *School Attendance Reports* — 180 school days—days absence due to colds, 1931-32: 11,426½ (registration 1,905); days absence due to colds, 1932-33: 10,625½ (registration 2,167); days absence due to colds, 1933-34: 9,261 (registration 2,122).

It is evident from consideration of Tabulation I that with an increased enrollment of 262 children, our records showed an 18 per cent reduction in days' absence due to colds during the first year in which our plans of prophylaxis were carried out.

(b) *Parents' Questionnaires*—These were sent to parents of those children who took halibut or cod liver oil during the winter months at home or at school. Of the 301 questionnaires returned, it was determined that to 225 children haliver oil was exhibited and 76 pupils were given cod liver oil.

The incidence and the severity of colds in those pupils to whom halibut or cod liver oil was administered are detailed in Tabulation II.

In the Fall of 1933, we found it to be impossible to continue dispensing haliver oil at school, but throughout the Winter all children were encouraged to take it or cod liver oil at home. When we compared the records for the third year with those of the first year, an improvement of 27 per cent was observed.

TABULATION II

The taking of one of these fish oils at home was discovered to be not so satisfactory as the regular giving of haliver oil at school. Studies by Sherman and Cammack (2) indicate that Vitamin A may be stored in large quantities in the body. The maximum quantity which the body can store is reached by a process of gradual accumulation. Many parents became discouraged when a child developed a cold after taking one of these fish oils several weeks and then discontinued the prophylactic remedy. Sometimes when the home supply of the oil became exhausted, several weeks would elapse before the mother purchased a new supply.

CONCLUSIONS

Because of the difficulty of controlling the outside factors of a demonstration of this kind, it is impossible to make an unqualified statement as to the efficiency of Vitamin A in cold prevention. However, we believe that Vitamin A added to the diets of our Long Beach school children has tended to increase their resistance to the common cold.

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ABSTRACTS

M. A. GOLDZIEHER, S. SHERMAN AND B. B. ALPERSTEIN.

Endocrinology. The Fat Tolerance Test in Pituitary Disease. 18:505-512, July-August, 1934.

A fat tolerance test has been devised to demonstrate the functional state of the anterior lobe of the hypophysis as measured by the physiologic discharge of a fat metabolism hormone. The "measuring-rod" is the level of the blood acetone after ingestion of a fat test meal. It is the opinion of the authors after use of the test meal in 109 cases, that almost all of the 56 patients in whom there was an absence of the physiologic rise of blood acetone bodies after the test meal were affected with pituitary deficiency. The authors believe that the consistent combination of a low specific dynamic action, high uric acid and increased fat tolerance characterizes pituitary insufficiency.

Dwight L. Wilbur, Rochester, Minnesota.

E. H. RYNEARSON, M.D.

Hyperinsulinism; the Misuse of the Term. Proceedings of the Staff Meetings of The Mayo Clinic, Vol. 9, No. 39, September 26, 1934.

"Seale Harris, in 1924, first suggested the diagnosis of hyperinsulinism, but it was not until 1927 that Wilder and his associates reported the first proved case, that of a surgeon, suffering from acute attacks of severe hypoglycemia, who was found at operation to have a carcinoma arising from the islands of Langerhans, with multiple metastatic growths from which large amounts of insulin were obtained.

Since that time, many papers and reports of cases have been published under the general title of "Hyperinsulinism". Because of the importance of this interesting subject, and because of the many different syndromes which are being grouped under this term, it is well to define it.

By hyperinsulinism is meant a condition wherein hypoglycemia is caused by excessive production of endogenous insulin. Many cases have been reported in which this insulin was produced by a tumor of the islands of Langerhans, and some patients have been returned to health by removal of such a tumor. This history of such a patient is clear-cut and diagnostic, and can be illustrated by the first of the following reports of cases.

REPORT OF CASES WITH COMMENTS

Case 1—A laborer, forty-five years of age, had been in good health until four years before his admission to the Mayo Clinic. At that time he had begun to have symptoms resembling those of drunkenness. These had appeared between meals, had been much more likely to occur if he had worked hard, and had been relieved by taking food. On one occasion he had had a characteristic epileptiform seizure, followed by unconsciousness which had lasted sixteen hours. When he awoke, he had been mentally confused until he had drunk some milk, when his condition rapidly had become normal. About this time he and his friends had realized the value of food in relieving these symptoms, so that on another occasion, when he had been unconscious for twenty-six hours, a friend had revived him by forcing him to drink milk. He complained of a severe headache, in conjunction with these symptoms, which had persisted in varying forms through the entire four years.

The clinical diagnosis of spontaneous hypoglycemia was confirmed by a reading for blood sugar of 30 mg. per 100 c.c. At operation, a tumor of the island cells of the pancreas was discovered and was diagnosed carcinoma. Immediately following the operation, the concentration of sugar in the blood returned to normal, and hypoglycemia never recurred. The patient has been in excellent health and never has had symptoms of any sort since his operation in 1931.

Comment on Case 1, and on two cases of a puzzling type: In the history there are several important features: the patient's symptoms were present only when he was hungry, they often were produced by exercise, they were essentially of neurologic character, they were relieved by ingestion of carbohydrate, and they disappeared entirely following surgical removal of an adenoma of the island cells of the pancreas.

Hyperinsulinism is only one cause of spontaneous hypoglycemia. Other causes are listed by Wauchope as follows: 1.—Excess of insulin. This may be the result of therapeutic injections of insulin, of tumors and hyperplasia of the pancreas, or of functional hyperinsulinism (idiopathic hypoglycemia). 2.—Lack of opposing secretions. This condition may result from disease of the suprarenal glands, from tumors of the anterior or posterior lobe of the pituitary body, or from myxedema. 3.—Lack of glycogen. This lack may result from destruction of reservoirs, from disease of the liver or wasting of muscles, from abnormal secretion of sugar, from renal diabetes, from lactation, from active depletion of stores such as occurs in muscular exercise, and from failure to replenish stores as in starvation. 4.—Interference with regulating center. This may result from a nervous disease which affects the pons, or from overaction of the vagus nerves.

It can be seen that anything which interferes with any step in the complicated mechanism of carbohydrate metabolism may produce hypoglycemia. Judd, Kepler and I have described hypoglycemia caused by primary pathologic changes in the liver and J. Wilder has attributed the condition in two cases to lesions in the pituitary body. Unfortunately, the latter cause was not completely proved.

The group which is causing most confusion is illustrated by the cases of which reports follow:

Case 2—A woman was first admitted to the Mayo Clinic in 1912, when she was twenty-four years of age. At that time, a diagnosis of "neurosis" had been made. She was readmitted August 30, 1934, with the history that she had had average good health, except for symptoms of cholecystitis, until 1926 when migraine had developed. In 1929, following an attack of mumps, she had complained of weakness, tremor, dizziness and fatigue. In 1930 following her husband's death, her symptoms had increased in severity. In 1931 attacks had begun to develop which had consisted of blurred vision, sleepiness, weariness, numbness, palpitation of the heart, and mental confusion. The symptoms had had no relation to meals and hot cocoa had been the only food to effect relief. In January, 1932, she had had a severe attack of gallstone colic. At about this time, because of the nature of her complaints, her physician had suspected hyperinsulinism. Readings of glucose tolerance at the third hour had been respectively 50 and 60 mg. per 100 c.c. of blood, on two determinations. No determinations of blood sugar had been made during an attack. Because of the evidence related and the chronic cholecystitis, operation had been performed elsewhere in February, 1932, at which time the gall bladder and part of the pancreas had been removed. Six weeks later a reading of glucose tolerance at the third hour had been 100 mg. per 100 c.c. of blood. The woman had felt somewhat improved until June, 1932, when her mother had died and her attacks had returned. These had continued intermittently thereafter.

Examination at the Mayo Clinic gave essentially negative results except that renal glycosuria was discovered

The value of blood sugar fasting was 98 mg. per 100 c.c. and the reading of glucose tolerance at the third hour was 66 mg. per 100 c.c. She was dismissed with advice as to how to relieve her chronic nervous exhaustion.

Case 3.—This patient, a man, first had come to the Mayo Clinic in 1920 at the age of thirty-two years, because he had been rejected for enlistment in the army on account of the presence of a goiter. None had been found, and his complaints, largely of weakness, had been felt to be on the basis of neurosis.

The patient returned September 12, 1934, to report that shortly after he had left the Clinic in 1920 the attacks of weakness had become more pronounced; he gradually had noted their occurrence when he was hungry, and he had obtained relief by eating. These attacks had consisted of exhaustion, generalized aches and pains, dyspnea, sweating, dizziness on stooping over, salivation and mental confusion. For years before his admission he had been eating six to seven meals a day, but as he had not had trouble during the night he had not had to resort to nocturnal feedings. In March, 1930, he had consulted a physician who had obtained a glucose tolerance curve and had found the reading at the third hour to be 48 mg. per 100 c.c. A diagnosis of hyperinsulinism had been made, and the patient had been advised to have an exploratory operation on the pancreas. He had refused; he then had been advised that it was dangerous for him to continue as a machinist. He thereupon had begun selling papers but his attacks had continued.

On the patient's admission to the Mayo Clinic his reading of glucose tolerance at the third hour was 65 mg. per 100 c.c. The value for blood sugar, fasting, was 90 mg. per 100 c.c. and he was advised not to eat until his blood sugar level had been determined. Such determinations were made at intervals, and at no time was hypoglycemia found. Without his having taken any food for twenty-eight hours, the concentration of blood sugar was still 90 mg. per 100 c.c. Accordingly, the opinion was reached that his symptoms were functional and not the result of hyperinsulinism, and he was advised to return to his usual occupation. Because of his frequent desire for food, roentgenologic examination of his stomach and duodenum was carried out and a duodenal ulcer was found, for which medical measures were prescribed.

GENERAL COMMENT

In Cases 2 and 3, the history was too long for a tenable diagnosis of hyperinsulinism, the fasting value for blood sugar was normal, the patients did not experience difficulty without taking food at night, and in Case 2 definite relief was not obtained from eating.

I am of the opinion that patients of this type should not be said to have hyperinsulinism. Neither the history nor the findings are suggestive of overproduction of insulin. The underlying condition responsible for production of this syndrome is not definitely known, but it is probably a manifestation of a vagotonic disturbance. At the Clinic we have chosen to call this "functional hypoglycemia" to distinguish it from the group of cases of organic hypoglycemia caused by hyperinsulinism, cirrhosis of the liver and so forth.

There are repeated references in the literature to sugar-tolerance curves as being suggestive, or typical of hyperinsulinism. There is no such thing as a suggestive or typical curve. In some of our most severe cases of proved hyperinsulinism, normal or diabetic sugar-tolerance curves, and low values for blood sugar at the third hour of the sugar tolerance test are found in an appreciable number of cases in which there is no suggestion of hypoglycemia. In one year, more than twenty patients were found to have a reading for blood sugar at the third hour of 60 mg. per 100 c.c. or less.

In conclusion, I do not believe that the term hyperinsulinism should be made a waste-basket for vague and poorly defined conditions in which mild hypoglycemia, or an unusual glucose-tolerance curve, is a part of the picture rather than a cause of it."

Frank Smithies, Chicago.

YOSHIO ASODA.

Significance of the Liver in the Metabolism of Lipoid Bodies. Changes in Lipoid Bodies in the Blood and Bile When Various Kinds of Bile Acids Are Administered. Japanese Journal of Gastroenterology, Vol. VI, No. 1; April, 1934.

The study was suggested by the observation that liver disease brings about a definite change in the lipoid bodies in the blood and bile and that lecithin injected is not excreted by the pathological liver but is retained in the blood. Experiments were carried out to show the effect of the various bile acids in connection with the fat content of bile and blood. The peroral administration of bile acids to rabbits brings about, as a rule, a temporary decrease in lecithin, total cholesterol and total fatty acids in the blood. Continuous administration of bile acids also provokes a gradual diminution in these fatty bodies except that the total fatty acids present a temporary increase in the early period of the administration. Various kinds of bile acids were administered by mouth to rabbits with the following conclusions:

1. Lecithin, total cholesterol and total fatty acids are decreased in the blood.
2. Lecithin, total cholesterol and total fatty acids in the bile are increased in both concentration and amount.
3. The quantitative changes in lecithin and total cholesterol are parallel with each other in the blood and the bile.
4. These results are irrespective of the kind of the bile acid.
5. These facts corroborate the idea that the liver regulates the amounts of lipoid bodies in the blood by the control of their excretion into the bile.

V. C. Rowland, Cleveland, Ohio.

ACHARD, PROF. CH.; LEVY, JEANNE, ET GEORGIAKIS, N.

The Cholesterol of the Food. Arch. des Mal. de l'App. digestiv et des mal. de la Nutrition, Paris, Octobre, 1934.

After an extensive review of the important *rôle* played by the cholesterol in pathology, the authors, although believing it increases in the body when the diet is rich in cholesterol, claim that there exists a systemic regulation of the cholesterol depending on a physico-chemical phenomenon independent from the synthesis of this body. It is most likely of exogenous origin. There appears to be a cycle according to which the *vegetable cholesterol* is converted into *phytosterol* to become secondarily an *animal cholesterol*, when assimilated by the latter. And finally is eliminated as *coprosterol*.

Hypercholesterolemia may be alimentary or digestive. When digestive, its formation is slow. Still, the seat of the synthesis remains unknown. The cholesterol-rich diets being obviously forbidden to the patients suffering from a cholesterolemia, the authors have made a survey of the quantity of cholesterol contained in various food-products, by an improved original method. The lipoids of the same products have also been calculated.

To give an idea of a long list we point out the few following food-products as containing a high cholesterol content: milk, table butter (0.760 per 1000), olive oil, fresh cream, cream cheese, most of the cheeses, veal and mutton kidneys, calf's liver, calf's brain (19. per 1000), the yolk of the eggs (17.540), shrimps, oysters, brioches, peas, fresh nuts, peanuts, chestnuts, almonds and chocolate.

Jean R. A. Le Sage. Montreal, Canada.

The Differentiation of Confusing Shadows in Cholecystography

By

MORRIS A. HERSHENSON, B.S., M.D.
PITTSBURGH, PENNSYLVANIA

TO PRODUCE cholecystograms of maximum diagnostic value, it is necessary not only to obtain roentgenograms of excellent photographic quality, but it is important, also, to place the gall bladder image away from interfering superimposed shadows of other tissues in the vicinity. The technical quality of the roentgenogram is governed, first, by accurate centering of the dye-filled gall bladder, second, by correct exposure of the film to the roentgen rays, and third, by the proper processing of the roentgenogram in the dark room. This discussion will be limited to the first requirement of these three.

The advantageous placing of the gall bladder shadow in the picture is dependent upon the position of the patient on the X-ray table and the location of the source of light, that is, the position of the X-ray tube. One frequently finds the shadow of the gall bladder coinciding, in whole or in part, with the shadows cast by other structures, such as the ribs, spine, or gas-distended intestines. In order to isolate the gall bladder from this confusion, various refinements in cholecystographic technique have been offered. Most of these suggestions are concerned with the position of the patient. The usual is the posterior-anterior one, that is, with the subject lying horizontally on the table with his abdomen towards the film and his back towards the X-ray tube. Held and Goldbloom have stressed the value of the "left lateral-anterior" position. By rotating the patient on his left side through an arc of about thirty degrees, they permit the gall bladder shadow to fall, frequently, at a point on the film away from the transverse processes of the spine and away from the shadows of the kidneys and the denser portion of the liver. Recently, Akerlundt has recommended the taking of gall bladder pictures with the patient in the upright position also. This position permits the intravesical stones to drop down towards the fundus of the gall bladder, and so differentiates shadows produced by freely movable stones from those produced by fixed tumors of the gall bladder wall. An exception is found only when the specific gravity of a layer of bile within the gall bladder is as great as, or even greater than, the specific gravity of the stones, in which case the stones naturally will not sink below this layer of bile.

Yet with all these attempts to separate the gall bladder image from shadows cast by neighboring structures, and also to interpret accurately negative shadows within the gall bladder, two confusing interferences frequently persist. The first is caused by the shadow of one of the ribs overlying the shadow of the gall bladder or obscuring the cystic or common ducts. The second is caused by gas-distended intestines coinciding with part of the gall bladder image. This gas is frequently found in the hepatic flexure and also in the first portion of the transverse colon, as well as in some of the upper loops of the small intestine. If such a gas bubble lies over the edge of the gall bladder so that part of it is outside the boundary of the gall bladder image, its true character easily is recognized. But when a small gas bubble in the bowel casts its shadow entirely superimposed by the gall bladder shadow, it frequently simulates a radio-lucent intravesical stone. A third, though less frequent cause of confusion, may be produced by radio-opaque shadows cast by urinary calculi or by calcified mesenteric lymph nodes in the vicinity of the gall bladder.

If the shadow of the dye-laden gall bladder could be slightly displaced, to one side or the other, without disturbing the rest of the picture to a like degree, it would be a simple matter to see any portion of the gall bladder or duct previously hidden, or to interpret which shadows within the gall bladder margins are cast by intravesical calculi or growths, and which are produced by structures lying in a plane above or underneath the gall bladder itself. Shadows of stones within the gall bladder would always lie within the border of the image of the gall bladder itself, while others could assume a position as a whole or in part outside the margin of the gall bladder. The simplest way to produce this relative displacement of the gall bladder image with relation to the rest of the picture is not to roll the patient into a new position, but to move the X-ray tube as one would for the taking of stereoscopic pictures. The mechanism of this maneuver

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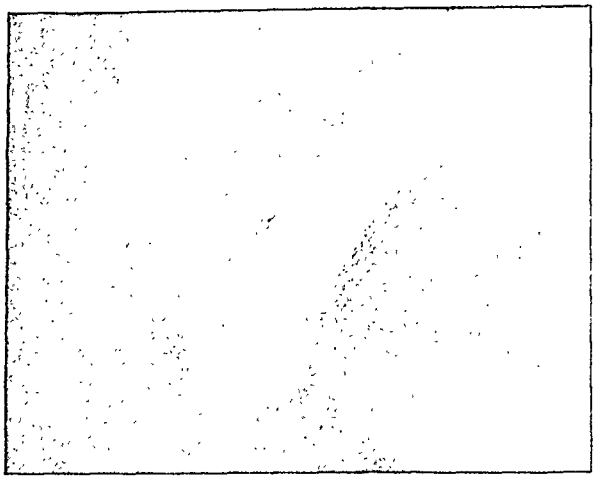


Fig. I



Fig. II

The illustration on the left shows a frequent occurrence where the shadow of the gall bladder coincides with the shadow of a rib. The illustration on the right shows the gall bladder shadow free of any superimposed shadows as obtained by shifting the tube as shown in Fig. V and VI.

is obviously simple and is illustrated by the accompanying diagrams. When the tube is moved from position A to position A′ (Figures V and VI), the shadows of those objects lying nearest the film are displaced the least distance, while the shadows of those objects lying farthest from the film are displaced the greatest distance. Thus, in the second illustration, the shadow of the gas bubble falls outside the margin of the gall bladder image, while the shadow of the stone is still within the margins of the gall bladder. This variable displacement is the physical basis for the production of stereoscopic pictures. The same effects, it is true, could be obtained by rotating the patient somewhat. As the tube can be brought into a definite, accurately measured location which can be duplicated for a new set of films, moving the tube is not only easier, but more exact than rolling a patient through an undetermined arc into a position which cannot be duplicated.

It is not my intention, however, to recommend the study of cholecystograms stereoscopically.

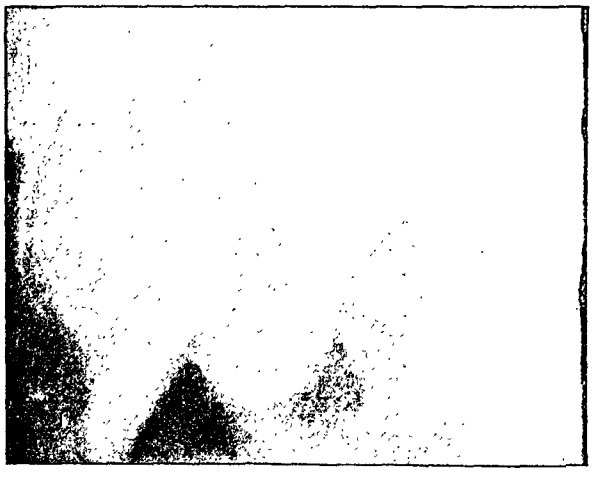


Fig. III



Fig. IV

The illustration on the left shows several shadows within the gall bladder boundaries, some of which simulate radio-lucent stones. But their true nature is shown by the illustration on the right which was made after the shifting of the tube. Several of the confusing shadows now extend beyond the margins of the gall bladder shadow and the one nearest the top which remains within the boundaries of the gall bladder has been shifted in position sufficiently to show that it must be located in a plane closer to the x-ray tube than the gall bladder itself.

Of course, one may do so if he chooses. What I propose is making two films in succession, and shifting the X-ray tube between these two exposures as would be done in making a stereoscopic set of films. Each picture so produced, however, is to be studied separately and shadows overlying the gall bladder image on each of them compared. Since these two films will be viewed singly, and since the desired effect is to displace the gall bladder in relation to the rest of the picture, I suggest that the X-ray tube be shifted about twice the distance commonly employed in stereoscopic technique. This greater shift will augment the displacement of the images on the films even more. Thus, for example, in Figure VII, OO′ represents the target-to-film distance, in this case, let us say, thirty inches. In making stereoscopic pictures, the tube would normally be shifted two and one-half inches. In order to produce an even greater displacement of the shadows, however, the first film is taken with the tube in position A, which is two and one-half inches from O, and the second film is taken with the tube at A′, which is two and one-half inches from O also. Thus the total shift of the tube is five inches. Normally, the tube is shifted in the direction of the grid, the same as one does in standard stereoscopic work. But in selected cases, the tube may be shifted perpendicularly to the direction of the grid in order that superimposed, confusing shadows may be better separated.

These suggestions are recommended to be used routinely in the making of cholecystograms irrespective of the position in which the patient is placed. The making of films in sets of two with the X-ray tube being shifted, will help to clarify the reading of cholecystograms no matter whether the patient is in the posterior-anterior, left lateral oblique, or the erect position.

SUMMARY

1. A refinement in cholecystographic technique is described in the making of roentgenograms in sets of two, the X-ray tube being shifted as in the making of stereoscopic films.

2. The X-ray tube may be moved to about twice the usual stereo-shift distance, since the resulting films are to be studied separately and not to be viewed in a standard stereoscope.

3. This procedure will separate the gall bladder shadow from the shadows superimposed upon it by neighboring overlying structures.

4. This technique is recommended to be incorporated routinely in cholecystographic studies irrespective of the selected position in which the patient may be placed.

Fig. V

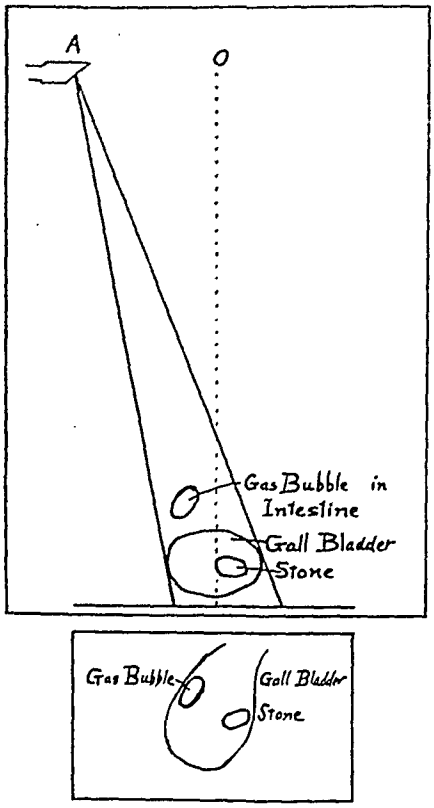


Fig. VI

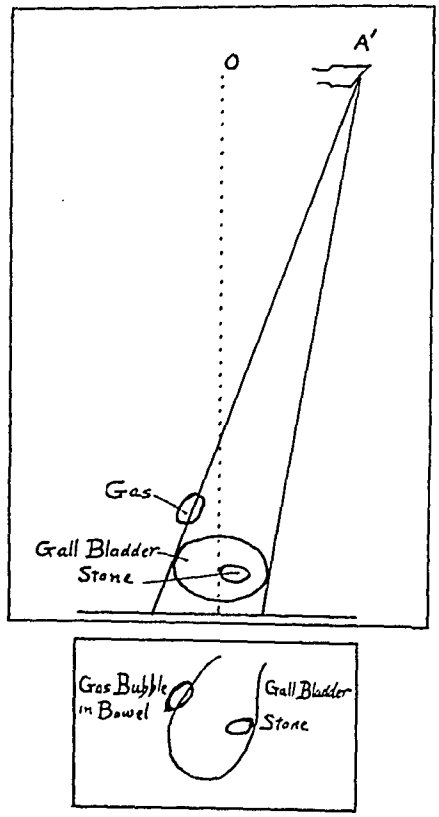
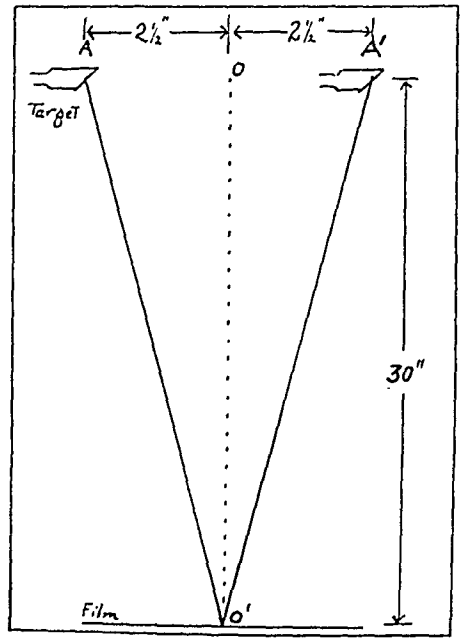


Fig. VII



ABSTRACTS

COLLINS, E. N., AND JONES, THOMAS E.

Benign Stricture of the Intestine Due to Irradiation of Carcinoma of the Cervix Uteri. S., G. and O., 59:644-649; October, 1934.

Another etiological factor is added to the long list of possible causes of intestinal obstruction. The authors, in reviewing a series of 422 cases of cervical carcinoma in which irradiation therapy was exhibited, found 6 patients (1.4 per cent) presenting the late complication of a benign stricture of the intestine. Five of the lesions were high in the sigmoid.

The symptoms (unusual constipation or intestinal hemorrhage) may appear in from several months to several years after the actinotherapy. Practically all the patients gave histories of unusually severe and prolonged rectal symptoms after the irradiation. Barium enemas proved the most important single means of demonstrating the lesion.

Even if these obstructive lesions are not preventable by proper technique (and most of them are) the incidence of post-irradiation stricture is too small to constitute a reason for not using such therapy. The important point is to remember the possibility of stricture so as not to be too prone to attribute symptoms arising after irradiation to metastasis. Abdominal exploration is warranted particularly where there is no remaining evidence of carcinoma in the pelvis. Surgical resection of the lesion is the treatment indicated.

The technique of proper roentgenological examination and proper irradiation therapy is given.

J. Duffy Hancock, Louisville, Kentucky.

KIRKLIN, B. R.

Duodenitis and its Roentgenologic Characteristics. Amer. Jour. Roent. and Radium Ther., May, 1934.

The author discusses the history, morbid anatomy, and clinical features of duodenitis. The roentgenologic aspects of duodenitis are excellently presented. From his aggregate experience the author presents the roentgenologic characterististics of duodenitis and states that first in importance among the signs is abnormally increased irritability of the duodenum, although this varies considerably in degree; namely, it is in direct ratio to the intensity and extent of the duodenitis. In typical instances the hyperirritability is manifested in intense spasticity and hypermotility of the duodenum. The barium races through so rapidly that there is scant opportunity to inspect the shadow. The bulb frequently is small and grossly deformed both on its mesial and lateral borders, and the configuration of the deformity varies quickly from moment to moment. Further, the bulbar shadow lacks the density commonly seen in cases of frank ulcer; it is thin and indistinct, and its margins are hazy.

A second characteristic is the mucosal pattern which is coarsely and irregularly reticular, and is depicted as translucent islets lying in a denser network.

A third characteristic of simple duodenitis is the absence of an ulcer crater. Neither marginal niche nor persistent central fleck can be seen.

Finally, uncomplicated duodenitis is marked almost invariably by absence of gastric retention or other evidence of obstruction, whereas such obstruction occurs in more than 25 per cent of cases of true ulcer. In the roentgenologic syndrome of duodenitis is a small, hypertonic stomach with active, sometimes disordered, peristalsis.

The article is very well illustrated and there is an abundance of reference.

D. S. Beilin, Chicago, Illinois.

WILCOX, LESLIE F.

Tertiary Syphilis of the Esophagus with Report of a Case Recognized Roentgenologically. Amer. Jour. Roent. and Radium Ther., June, 1934.

The author discusses briefly the literature on the subject as well as presents the pathological aspects. Wilcox states that tertiary syphilis of the esophagus is relatively rare and usually terminates in stenosis of the lumen of the esophagus, as much as one-half or more of its length being involved. The chief symptom is dysphagia which accompanies the slowly developing stenosis. He states that the roentgenologic study is of the greatest importance in the diagnosis and serological tests and esophagoscopy should always be a part of the examination. Intensive antiluetic treatment must be carried out. Owing to the marked fibrosis in the healing of the lesion the stenosis is more or less permanent and instrumentation may have to be resorted to over a long period of time in order to dilate the involved portion of the esophagus.

The article is illustrated by a case and includes several roentgenograms showing the result of antisyphiletic treatment.

D. S. Beilin, Chicago, Illinois.

BUCKSTEIN, JACOB.

Roentgenologic Evidence of Healing of Jejunal Ulcer. Am. Jour. Roent. and Radium Ther., October, 1934.

The author discusses the value of the niche in the roentgen diagnosis of peptic ulcer and states that it has been clearly established since the original observation of Reiche, in which a mushroom-shaped protuberance of the lesser curvature of the stomach in the roentgenogram was shown on autopsy to correspond to the presence of a gastric ulcer. Similar evidence was eventually shown to be reliable in the diagnosis of both duodenal and jejunal ulcer.

He further states that not only was the niche of great value from the standpoint of diagnosis, but it served as an objective criterion, for the determination of the therapeutic effectiveness of medical treatment, by the demonstration of retrogressive changes in the size of the niche or its eventual total disappearance. He states roentgen evidence of the disappearance of a niche need not, it is true, indicate actual anatomical disappearance of the ulcer.

Buckstein also discusses the pitfalls in the roentgen diagnosis by emphasizing that prolonged and repeated careful roentgenographic examination with proper technique will minimize the possibility of error. He states that the niche of the jejunal ulcer may be favorably influenced by medical treatment as is shown by some excellent case reports illustrated with roentgen studies.

D. S. Beilin, Chicago, Illinois.

SECTION V—*Therapeutics*

The Treatment of Massive Gastro-Duodenal Hemorrhage

By

FRANK SMITHIES, ScD., M.D.
CHICAGO, ILLINOIS

MANAGEMENT of gastric hemorrhage, in order to be successful, depends upon an accurate appraisal of the condition responsible for the initiation and maintenance of the hemorrhage. Particularly does this apply with respect to therapeutic operative procedures contemplated toward the abdominal viscera.

HISTORY NOTES

First, a brief history of the patient's past and present constitutional and digestive difficulties should be obtained—preferably not from the patient (except in emergencies) but from attendants or relatives. Commonly this can be done while the patient is being placed in bed or taken to a hospital.

IMMEDIATE THERAPY

Without loss of time, especially when lesions of the abdominal viscera are known to exist or are suspected, a hypodermatic injection of one-fourth to one-half grain of morphine sulphate with or without atropin should be given. Where hemorrhage is copious and there are marked retching and vomiting or when a patient is restless and noisy, there is no drug so valuable as morphine in physiologic doses in the emergency treatment of hemorrhage—it lowers blood pressure, slows the heart, relaxes muscles systemically and locally, quiets nervous or hysterical patients and assures complete bodily rest. Much larger doses than are commonly given should be employed—even up to a half to a grain every two or three hours for several doses. The main contraindication to the exhibition of large or frequent doses of morphine is slowing of the respiration to 10 or less per minute. When morphine is given frequently, atropia should be used cautiously or omitted. The too frequent exhibition of atropia results in diminished urine output or even anuria and the attendant dryness of mucous surfaces and skin are distressing to the patient. In "shocked" patients or in subjects where the surface circulation is poor, subcutaneous injections of morphine rarely are effective because they remain locally where injected, instead of getting into the systemic circulation. In such circumstances, it is our custom to give morphine *intravenously*. When it is thus exhibited, the dosage should be from one-fourth to one-third of that commonly given subcutaneously. Morphine or codein administered intravenously very often prove much more efficient than when given by any other route, so much so that, unless there are contraindications to morphine or codein, in general, when hemorrhage is brisk, almost uniformly the first injection which I give of either of these sedatives, is by the intravenous channel.

Submitted November 9, 1934.

REST

It is not necessary to emphasize that the patient should be put to bed, and kept there, external heat being supplied liberally and the central nervous system stimulated by the head and shoulders being low. This can be accomplished by elevating the foot of the bed on ten-inch blocks. This position not only favors normal cerebral circulation but permits vomiting without effort and prevents regurgitation of vomited material into the bronchi. Particularly is regurgitation avoided if patient is inclined onto the left side and the head placed low and turned to the left.

EXAMINATION

After this initial treatment has been instituted, with the patient stripped, there should be carried out, in every instance, a rapid physical examination, no part of the body from the head to the toes being neglected. Such examination commonly gives indication as to the source of bleeding: whether hemorrhage has resulted from venous stasis, concomitant with heart malfunction, from liver cirrhosis, pulmonary lesions, anomalies of the spleen, biliary tract and pancreas, abdominal trauma or intragastric or intraintestinal lesions. In all instances, whether or no an abdominal focus of disease is located or suspected, the male patient or his relative should be questioned with regard to the hemophilic taint.

The *blood pressure* always should be taken, not only to secure a relative appraisal of deficiencies of heart strength and blood volume, but in order to establish a point from which subsequent blood

pressure readings may be contrasted in patients who go into shock or continue to bleed.

Should the patient be in a hospital, *complete blood counts* should be made immediately and the blood clotting time estimated by such reliable procedure as that of Thomas Boggs.

HOT SOLUTIONS FOR GASTRIC LAVAGE

If vomiting is copious, and particularly if it is accompanied by much retching and the appearance of large blood clots, then by means of a large bulb-free stomach tube, *thorough lavage* should be performed with normal salt solution at a temperature of 110° Fahrenheit, as suggested by the late Dr. Rodman. This procedure is remarkably efficacious in stopping hemorrhage and putting the stomach at rest. So long as large clots are in the stomach, peristaltic activity will continue in an effort to get rid of or digest them. Such mechanical activity on the part of the stomach interferes with protective clot formation at the site of intragastric bleeding. The heat of the lavage solution acts as an admirable hemostatic agent. In cases of actual or potential perforation, the emptying of the stomach lessens the danger of peritoneal contamination by food residues and blood. Where frank perforation has existed, free lavage after Rodman's method, with the patient in a partial Trendelenberg position, rapidly empties the stomach and renders subsequent operative procedures less hazardous. Our experience with lavage with heated solutions in patients exhibiting gastric hemorrhage is extensive: we have never observed any harmful effects. In many instances, it has seemed that lavage after this fashion served as a life-saving measure.

TOPICAL APPLICATIONS TO THE ABDOMEN

Many years ago, I abandoned the routine application of ice-bags and ice water-coils to the abdomen in patients where hemorrhage was suspected of coming from gastric or duodenal lesions. In our opinion, and from our clinical experience, the local application of ice is detrimental: it chills an already shocked patient, systemically as well as locally; it lowers body temperature and interferes with adequate central nervous system function; it has relatively little, if any, effect toward "constricting" blood vessels or capillaries and thus lessening bleeding—in fact, quite likely continued cold applications paralyze the vascular neuromuscular mechanism and by preventing normal constrictor action, prolong a hemorrhage which otherwise might cease spontaneously. One has but to scratch his hand and place over the bleeding scratch a piece of ice in order to prove how long bleeding continues following cold applications. Only in instances where physical examination indicates that perforation actually is taking place or has occurred and the peritoneum has been subjected to mechanical or infectious traumata, do we employ cold abdominal applications. In such circumstances, they are used in an attempt to immobilize a part and to lessen peritoneal engorgement. Frequently such measures permit limitation of an inflammatory process to such extent that later, at an opportune time, abdominal exploration may be performed safely.

For years, I have favored extremely *hot moist applications* over a suspected bleeding focus. Usually these applications were employed as hot compresses rather tightly bound upon the abdomen and frequently renewed. The tight fixation of the compresses limits the motion of the abdominal wall and lessens visceral peristaltic activity. The heat prevents shock; possibly it has a derivative action upon the capillary bed and if the compresses are sufficiently hot and moist, stimulates blood coagulation. The advantage of heat over cold as an agent toward improving the patient's feeling of well-being, is self-evident.

NOURISHMENT

Mouth feeding in all its aspects should be strictly interdicted. So long as the patient is ingesting material into his stomach, gastric peristalsis is stimulated, and with this stimulation of peristalsis, permanent clot formation is attained with difficulty. The sucking of ice, the drinking of ice water, the administration of such hemostatic agents as adrenalin solutions (liquid, gelatine or otherwise) or the effort to improve nourishment by exhibiting gruels, soups or so-called "ulcer diets" can be productive only of harmful effects. An empty stomach rapidly becomes peristalsis- and secretion-free, and if the viscus remains empty for longer than twelve hours, muscular contraction of the wall mechanically compresses bleeding capillaries or arterioles and lessens or completely stops hemorrhage. All too often, attempts at feeding or at administering medicinal and dietetic ulcer regimes initiate or prolong emesis and aggravate the local pathologic condition responsible for hemorrhage.

If bleeding is due to such local pathology as peptic ulcer, and if hemorrhage has been repeated or is continuous, one must recall that perforation is a strong possibility; hence attempts to administer food or medicine by mouth are a potent influence toward precipitating perforation. This observation can be substantiated readily by a short residence at any busy gastro-enterological or surgical clinic. There is no doubt that many patients who succumb suddenly to "acute indigestion" are instances where the cause of death is acute perforation of an ulcer or cancer; and this most serious accident would have been avoided had "routine" ulcer treatment orders, so common to many hospitals, not been carried out. It is our practice not only not to administer water, food or therapeutic agents by mouth during the acute stage of gastric hemorrhage, but to interdict anything but small sips of very hot water for at least two days after definite proof is available that hemorrhage has ceased and that the local abdominal examination indicates that peritoneal involvement is not present.

Feeding for the first few days of gastrorrhagia,

unless the patient is in extremely low general physical condition, is not especially needed, provided measures are directed to maintaining body fluids. McVicar and others have shown how essential it is that body fluids which are lost by hemorrhage or by persistent vomiting be replaced if one is to avoid toxic crises. We have never hesitated early to increase the fluid content of the body by all known available routes: intravenously, subcutaneously, or *per rectum*. Commonly, sufficient fluid can be given *per rectum* by the Murphy drip to replace fluid lost by bleeding, to prevent renal stagnation, to keep moist the mucous surfaces, particularly of the mouth, and to counteract shock.

AUTHOR'S NUTRIENT CLYSMA

For more than twenty years, we have employed as a nutrient enema the following: 8 ounces of normal salt solution; 30 c.c. of glucose syrup and 30 c.c. of 50 per cent alcohol. This is administered, at body temperature, and by the Murphy drip. The whole quantity generally is given four times within twenty-four hours. Medicinally, agents such as atropine, bromides, morphine, digitalis or even calcium may be added to these clysmas with beneficial results. Where the blood coagulation time is delayed, and bleeding, particularly profuse seepage of blood, occurs, we do not hesitate to give, intravenously, several times during twenty-four hours, 200 c.c. of one per cent solution of sodium bicarbonate and 20 c.c. of five per cent calcium chloride. Where the patient seems to be in poor flesh, in addition to being dehydrated, the sodium bicarbonate solution is supplemented by glucose in the proportion of approximately two per cent. In instances where rectal feeding is poorly borne and where it is difficult to administer fluid intravenously, normal salt solution can be administered at convenient places, subcutaneously, in large quantities, provided local tissue pressure from administered fluids is avoided.

Mouth-feeding should be begun only when there is conclusive evidence that hemorrhage has stopped and has not recurred. An increasing blood pressure, a lowered pulse rate whose quality is improved, a stationary or increasing red blood count and hemoglobin estimation are sufficient clinical evidence that hemorrhage no longer continues, especially, if the patient exhibits physical well-being, is free from pain or nausea and has a flat, soft epigastrium. "Occult blood tests" may be positive in the stools for many days after hemorrhage has stopped on account of retention, and if mouth-feeding is interdicted until occult blood tests are negative, then the patient is quite likely to have his resistance greatly reduced by lack of food, but, what is more important, to have his body fluids diminished below the safety point.

It is well not to feed by mouth until two days following cessation of hemorrhage. When mouth-feeding is begun, then a few simple but fundamental principles should be followed. Food should be administered in *small quantity frequently* and, to avoid gastric spasms, should be *given warm; foods which do not stimulate acid secretion should be chosen,* namely, carbohydrate mixtures in preference to mixtures of protein (milk, eggs, etc.); all foods should be selected with the idea of their leaving the stomach almost immediately, in order not to excite peristalsis or locally traumatize an injured area. One should be sure that the vitamin content of the food administered is adequate. Fruit and vegetable juices or thin broths prevent vitamin lack. Thin suspensions of yeast with or without solutions of haliver oil with viosterol usually are well tolerated if mixed with soups or gruels.

It is our policy to give no milk unless it is citrated or parboiled: "Raw" milk results in tough casein clots, and these clots excite the stomach to effort, both secretory and muscular, just as strenuously as if the patient were given meat to eat. If milk be used at all, it should be parboiled or mixed with an equal quantity of barley water in order that small flocculent casein clots result, or to each ounce of milk one grain of sodium citrate should be added. Condensed milk or milk powder in water solution are preferable to unaltered milk. Personally, I exhibit little milk or milk mixtures.

Generally, our feeding routine is two to four ounces of water gruel (made from barley, farina, cream of wheat, oatmeal, etc.), every hour, and at alternate hours an ounce of sweet fruit juice. After the first twenty-four hours, to the water-gruels may be added thin custard, strained soups, made from fresh vegetables or the now available strained or puréed vegetable mixtures marketed in tins (Libby's). This type of feeding supplies adequate vitamin demands, is readily borne, does not excite peristalsis or stimulate secretion, and its caloric value can be so computed that the diet can be built up rapidly from 400 calories to 1,800 calories daily. This quantity is quite sufficient for the average individual in bed at rest. When the nourishment demands are increased, then thin cereals, purées from potato, peas, beans, carrots and other vegetables and small quantities of chopped meat, particularly liver, kidneys, sweetbreads and calves' brains, may be exhibited. For at least two weeks following a hemorrhage, one should be sure that the calories are kept below 3,000, and that at least six feedings daily are given.

Charts of pulse, temperature and blood pressure should be kept, in order that one is reassured that bleeding has not recurred. If the patient is in a hospital, certainly the hemoglobin and the blood count should be estimated every day.

Even after the patient has gained strength and energy and is up and about, for months he should be cautioned against an excess of protein or fat (the fat slowing the emptying rate of the stomach) and should avoid "roughage feeding" in every form. After the first or second hemorrhage, patients frequently gain weight very rap-

idly. This should not be allowed, inasmuch as should an acute emergency arise from another hemorrhage, with or without ulcer perforation, the operative risk upon an obese individual is very grave.

PATHOLOGIC SIGNIFICANCE OF MASSIVE BLEEDING IN PEPTIC ULCER

Particularly to individuals who have had hemorrhage from bleeding gastric or duodenal ulcer, definite information regarding the nature of the ailment and its possible consequences should be given. It should be emphasized that a patient who has had one severe hemorrhage is likely to have another, and that each succeeding hemorrhage is likely to be more severe. Furthermore, the anatomic consequences of hemorrhage should be mentioned—namely, that with each succeeding hemorrhage there is a greater destruction of the gastric or duodenal wall and that it is not possible to tell when this destruction will advance to the stage where the wall of the viscus completely is destroyed and perforation result. It has always been my custom to tell a patient who has had one severe hemorrhage that he is potentially a subject for surgery. No physician is able to determine in any given patient whether or no he will have another hemorrhage, or how soon there may be a recurrence. Neither is a physician able to tell in any given case the consequences of hemorrhage—whether an uncontrollable "spurter" will be opened, whether perforation will occur immediately or within a short time or whether the extension of the ulcer will involve to a dangerous degree an adjacent viscus. In the circumstances, it is only fair to any subject that the true condition be explained to him, and, provided the bleeding does not result from a blood dyscrasia, or during a physiologic cycle such as the menopause, or in association with a disease not definitely ascribable to the stomach or duodenum, surgical exploration and treatment should be insisted upon. Frequently, such course of management is refused by the patient, but if the physician has made his viewpoint clear and the patient understands it and is willing to assume the risks, then the physician is relieved of much responsibility in the carrying out of any regime other than surgical. It is astonishing how frequently, however, both patients and physicians are ready to gamble upon the future, when the patients have already experienced one severe gastric or duodenal hemorrhage. While this may be human nature, yet when crises occur the patient who is turned over for surgical management is in a far more hazardous state than he would have been had surgical intervention occurred at a time when his general condition was excellent and what had to be done surgically could have been carried forward in a leisurely and scientific manner.

THE STOPPAGE OF BLEEDING BY DRUGS

In my experience never has this been very successful. This may be due to the fact that I have not used many drugs for such purpose but rather, by keeping the patient at rest in bed, stopping peristalsis by morphia, supplying sufficient fluid to stimulate cerebral activity and keeping the stomach free from food, etc., I have not had to employ many of the commonly administered local hemostatics. Not rarely, one hears of good results following the introduction into the stomach of such mixtures as adrenalized gelatin, adrenalin solutions, tannic acid solutions, etc., etc. The use of adrenalin intramuscularly or the intramuscular administration by the hypodermatic route of coagulating agents such as thrombo-plastin, coagulose, horse serum, etc., has been favorably recommended. Certainly, if these agents are not administered in such quantities as to cause harm, one may employ them on the general theory that they may do good, or that, if the case should turn out badly, these agents having been administered, the physician's conscience is clear, inasmuch as he has exhibited all known remedies to prevent a catastrophe. However, no one yet has shown just how large a quantity of the above agents it is necessary to give to any individual or to any group of individuals, in order to stop gastric or duodenal bleeding, whether that bleeding be due to seepage or to free bleeding from an arteriole or an artery. Further, I have always felt that the administration of the above-mentioned agents leads to a sense of false security, and that while these agents were being pumped into the patient, bleeding was progressing to the point where serious loss of blood might take place or the continued bleeding extend such lesion as an ulcer to the stage of fatal perforation.

In my experience, the most potent agents to stop bleeding when the bleeding was not from a "spurter" have been the intravenous administration of 20 c.c. of five per cent calcium chloride solution every two hours for six doses, or, better still, prompt *transfusion of large volumes of whole blood* after the method of Kimpton-Brown, Percy. If these do not stop bleeding within thirty-six to forty-eight hours, it is evident that one has to do with a condition where it would be wise to urge surgical exploration without delay. Such exploration may reveal a bleeding malignant ulcer, an arteriole dripping constantly, or an artery from which an obstructing blood clot has been dislodged.

It has been advanced by individuals, quite carelessly and without clinical or laboratory proof, that blood transfusion tends to prolong hemorrhage by increasing blood pressure or by dislodging clots from the mouths of arterioles or arteries or by both. In a rather extensive clinical experience, I have never seen any ill effects following the massive transfusion of whole blood; but I have seen instances where neither blood transfusions or any other measure permitted the formation of an obstructive clot at the mouth of a "spurter" of fair size. The opinions which have been advanced regarding how much massive whole blood

transfusion (and I speak of "whole blood" transfusion because it has never been our policy to use citrated blood or blood altered in any other manner) increases blood pressure or dislodges clots, have been repeated by one clinician after another, without there seeming to have been, so far as I can learn, any basis of fact for these opinions.

In order definitely to learn just what effect increase in blood volume or increase in blood pressure has upon a freely bleeding vessel, at my suggestion, Dr. Ralph A. Kordenat carried forward a series of experiments. Working with fairly large dogs at the Research Laboratories at the University of Illinois, Dr. Kordenat and his associates exposed arterioles and arteries, severed them and permitted free bleeding and subsequent clot formation at the mouths of the vessels. The intravenous introduction of fluid in quantity sufficient almost to "water-log" the dog did not dislodge the clot, nor did the hemorrhage recur when the blood pressure had been raised, mechanically or by the use of adrenalin, to more than double the normal blood pressure. Furthermore, quantities of fluid, intravenously introduced and comparable in proportion with body weight or with the animal's normal fluid content, added to such amounts of blood as would be introduced during a therapeutic transfusion, resulted in but a very slight and transient rise in bood pressure, and had no effect whatever with respect to producing a recurrence of hemorrhage. These experiments, conducted by Dr. Kordenat and his associates, would seem to be of the greatest importance in demonstrating the harmlessness of whole blood transfusion as therapeutically carried out in the control of visceral hemorrhage, and should be of great assurance to physicians to transfuse, promptly and frequently, individuals whose visceral hemorrhages are not controlled by general and visceral rest. These experiments substantiate completely our clinical experience with regard to therapeutic transfusion of whole blood, and also the intravenous exhibition of saline solutions and calcium chloride.

Persistence of visceral bleeding usually indicates pathology that warrants surgical exploration. Too often, patients are permitted to die from exhaustion, shock or anemia, because bleeding is allowed to continue uninterruptedly, while futile efforts, therapeutically or dietetically, are being made to stop hemorrhage, nourish a patient or "build up the blood". As I mentioned above, *should an increasing pulse rate, a falling blood pressure and a falling blood count and hemoglobin estimation continue, the patient should be explored by a competent surgeon while he still is a fair surgical risk.* Not infrequently, a persistently bleeding ulcer can be excised or enfolded, a "spurter" ligated or a small malignant ulcer excised, largely under local anaethesia, and within a few days the patient is past danger and has a fairly encouraging outlook. Furthermore, this prompt action not rarely prevents perforation and fatal hemorrhage or peritonitis.

ROENTGEN EXAMINATIONS IN THE PRESENCE OF MASSIVE BLEEDING

Thus far, I have not mentioned the use of the X-ray as an aid in determining the pathology responsible for gastrorrhagia. Purposely I have not mentioned the X-ray, hoping that it would be self-evident that X-ray investigation had little place in the location of pathology productive of gastrorrhagia. Certainly, in acute hemorrhage or in persistent seepage, one should endeavor to forget that the X-ray method of investigating the alimentary tract ever has been devised. Every year, it has been my misfortune to observe individuals who have experienced acute gastric hemorrhage and upon whom, even while bleeding persisted, the X-ray method of investigation has been employed. In many of these patients, the heavy barium mixtures have not only prolonged hemorrhages and made them more severe, but in several instances the consequences have been fatal on account of resultant perforation. *It is our policy never to study a patient by means of barium mixtures until at least four weeks following proof of cessation of a severe hemorrhage.* Even then, one should proceed cautiously with both the fluoroscopic and the film studies. Certainly, the use of the X-ray method while a patient still is bleeding subjects the individual to hazards which no roentgenologist or clinician should be willing or anxious to assume.

For the guidance of house officers in all hospitals, there should be displayed, prominently, cautions that individuals who are brought into the institutions during gastrorrhagia or in whom gastrorrhagia later appears, *should not be X-rayed without the written permission of their chiefs.* If, from clinical history, physical examination and the various simple laboratory tests which have been outlined above, a workable appraisal of the condition to be treated cannot be made, certainly, little of value will be added to the picture by roentgen studies, and most assuredly the patient will be subjected to risks out of all proportion to any information which may be gained.

ABSTRACTS

MAHLO.

Is the Treatment of Gastric Ulcer by the "short wave" radiation indicated? Deutche Med. Woch. T. LX, No. 11, 1934.

In most of the cases of ulcer the short wave treatment created a favorable "terrain" for a definite cure. However, caution is necessary and the radiations must be limited in their quantity, otherwise they may cause hemorrhage. The sedative and analgesic effect of the treatment is unquestionable, but its curative value cannot be confirmed.

Jean R. A. Le Sage, Montreal, Canada.

SECTION VI *Abdominal Surgery*

"Silent" Carcinomas of the Large Intestine*

By

E. LEE STROHL, M.D.

and

J. A. BARGEN, M.D.

ROCHESTER, MINNESOTA

FROM time to time, we have observed patients at examination in whom carcinomas of the large intestine accidentally were discovered. This observation has been made frequently enough to arouse curiosity as to the incidence of such growths, why they occurred, where in the bowel they were most frequent, with what pathologic entities they might be confused and their pathologic types. Some of these, and similar questions led to this statistical study.

The records of 1,100 patients with carcinoma of the large intestine, who had been examined at The Mayo Clinic between the years 1924 and 1927, inclusive, were reviewed. During these four years, 621 of these patients were operated upon for the colonic lesions. Forty-two of these patients (6.7 per cent) had had no symptoms referable to the intestinal growth. "Silent" we have chosen to call such carcinomas.

The *ages* of these patients with silent carcinomas were slightly higher than were those of patients who had lesions of the upper part of the gastro-intestinal tract. The youngest patient was thirty-six years of age and the oldest was seventy-eight years. Fourteen (33 per cent) were between the ages of sixty and seventy years; whereas twenty-five (59 per cent) were between the ages of fifty and seventy years. The age distribution of the entire group was as follows: 35 to 40 years, four patients; 40 to 50 years, eight; 50 to 60 years, eleven; 60 to 70 years, fourteen, and 70 to 80 years, five patients.

There was but little difference in the distribution by *sex;* twenty-five patients were males and seventeen were females.

Ten of the forty-two patients had recorded family histories of carcinoma. A man, aged fifty-seven, traced three instances of carcinoma in his immediate family: his sister and mother had died from carcinoma of the breast and one uncle had died from carcinoma of the stomach. Another man, aged sixty, gave a history of having had one sister, one aunt, and one uncle, all of whom had died from carcinoma of the stomach. Seven of the ten patients, who had given histories of carcinoma in their families, reported that more than one relative had died of carcinoma.

By the term *"presenting symptoms"*, the subject of which we shall now consider, we mean those subjective complaints which were elicited by questioning for the chief complaint. Of the forty-two patients who had no symptoms referable to the intestinal growth, nine presented symptoms suggestive of disease of the gall bladder. Of the nine patients who gave histories of trouble referable to the gall bladder, six had been deeply jaundiced, one or more times, within a year preceding admission to this Clinic. A history of a case exemplifying such a condition follows:

> A white man, aged sixty-five, came to this clinic complaining that he had had acute "colic" in the right upper quadrant of the abdomen, eight to ten times in the past year, and that he had had jaundice six months before admission. He had dyspepsia after eating aromatic vegetables, starches and fatty meats, with bloating after meals. The bowels always had moved regularly once a day. The patient never had passed any blood with the stools.
>
> *Roentgenologic studies* revealed a non-functioning gall bladder containing stones. Roentgenograms of the colon were not made and proctoscopic examination was not carried out. *Erythrocytes* numbered 3,300,000 per cubic millimeter of blood; the concentration of hemoglobin was 14.1 gm. per 100 c.c. of blood. *Urinalysis* disclosed nothing of significance. A *clinical diagnosis* was made of chronic cholecystitis with stones.
>
> *Surgical exploration* revealed carcinoma of the hepatic flexure; the neoplasm measured 5 by 4 by 4 cm., grade 2 (Broders' classification), with extensive involvement of the peritoneum and lymph nodes, and with metastasis to the liver. Also there was chronic cholecystitis with multiple stones. Mikulicz's operation was performed. The patient recovered temporarily, but died three months after the operation from metastatic growths. In analyzing the history, after operation, it was disclosed that there had been an epigastric swelling following each attack of colic in the right upper abdominal quadrant, but the swelling always had disappeared in two to three days subsequent to the acute disorder.

*Respectively, from the Divisions of Surgery, Mayo Foundation, and of Medicine, Mayo Clinic.
Submitted November 15, 1934.

Seven of the forty-two patients gave "stomach trouble" as their presenting symptom. This disorder was indicated by "halitosis" in some; in others, it was featured by "sour stomach", bad taste in the mouth, and eructations and bloating following intake of food. Seven patients came to the Clinic complaining of general weakness and malaise, symptoms which had been present for periods of from three to twelve months before admission.

Six patients came to the Clinic complaining of *abdominal tumor*. Four of these tumors had been discovered by the patients themselves, whereas two had been discovered by family physicians. The following history exemplifies this group of patients:

A white man, aged thirty-seven, came to this Clinic complaining of a mass in the right lower quadrant of the abdomen, which he had found six weeks previously. The bowels had been regular; they had moved once a day without passage of blood.

The *erythrocytes* numbered 4,880,000 per cubic millimeter of blood and the concentration of hemoglobin was 15.9 gm. per 100 c.c. of blood. *Proctoscopic examination* was not made. *Roentgenologic studies* revealed a filling defect of the transverse colon, which was thought to be the result of carcinoma. *Urinalysis* disclosed nothing of significance. The *clinical diagnosis* was carcinoma of the transverse colon.

The patient was *operated upon*, and a carcinoma, which measured 9 by 8 by 6 cm. was removed and was graded 4 (Broders' classification); the regional metastatic involvement was graded 3. Lesions were not found in the liver. An obstructive type of resection was performed and the patient was living and well one year after operation. We have been unable to trace him since that time.

The *presenting symptoms* of one man, aged forty-one, were burning on urination and pain in the urethra, which occurred with bowel movements. At times prior to voiding, the patient had passed bubbles of gas through the urethra. One patient came to the Clinic on account of asthma, and, in the course of the examination, an abdominal tumor was discovered. This proved to be a carcinoma of the transverse colon. Another patient came to the Clinic stating that he had swallowed a tooth one year before. Six days afterward he had passed a small amount of blood, and on three or four occasions in the following year, he had passed small amounts of blood which he had attributed to the tooth which he had swallowed. The patient felt perfectly well, but wanted an investigation carried out to determine the position of the swallowed tooth. In two instances attention was directed to the colon because of secondary anemia which previously had not been explained; on studying their colons, roentgenologically, carcinoma was discovered. The presenting symptoms varied in the remaining eight cases, but in none did it suggest any intestinal condition.

The *intestinal habits* of this group of forty-two patients were not unusual. Five of the forty-two stated that they had had from two to five bowel movements daily; three of them had had such habits for five to seven years, and two of them for fifteen to twenty years. Thirteen stated that they always had been constipated, five of whom had been constipated only occasionally, however. Twenty-three always had been regular in their intestinal habits; the bowels had moved once a day, without passage of blood at any time. One patient stated that she had had diarrhea each Autumn for the past fifteen years, "during plum season".

Eleven of the group of forty-two patients were examined proctoscopically. A diagnosis of carcinoma of the sigmoid was made in five cases by such procedure. Roentgenologic study of the colon was advised in three cases, by the proctologists, and the carcinomatous lesions readily were demonstrated.

Roentgenologic examination proved to be of the greatest aid in localizing the lesions. Of the forty-two carcinomas, five were found in the sigmoid, three in the transverse colon, and nineteen in the ascending colon.

Six of this group of forty-two patients had submitted to operation elsewhere within a period of two to seven months prior to visiting this Clinic. Two came exhibiting postoperative fecal fistulas which had been present for from five to seven months respectively; an appendectomy had been done in each instance at the time of the previous operation. Three patients had undergone appendectomy two to four months before admission to this Clinic. One patient had submitted to cholecystectomy elsewhere, two months earlier.

Of the forty-two patients studied, twenty-one (50 per cent) had intra-abdominal *metastatic dissemination*. Twelve had metastatic lesions in the liver, seven in the omentum and two in the omentum and peritoneum. Two of this group had more than one malignant lesion. One man, aged forty-five, had had an epithelioma of the lip excised two years previously, while a woman, aged sixty-four, had had colloid carcinoma, grade 1 (Broders' classification), of the cecum and rectum. This latter patient was the one who had had diarrhea each Autumn for fifteen years, "during the plum season"; otherwise, her intestinal habits always had been normal; she had had one movement a day, without passage of blood. Three of these lesions had caused intussusception; two were situated at the ileocecal valve and one in the sigmoid.

Pathologically, this group of patients is most interesting. Twenty-one patients were discovered to have involvement of the lymph nodes. Specimens were removed in twenty-three cases of the group. The largest lesion measured 13 by 9 by 1.5 cm.; this was discovered in a man, aged sixty-one, whose chief complaint was "stomach trouble" which had lasted for one year. His bowels had been regular and had moved once a day. The smallest lesion, which was 3 by 2.5 by 2 cm. in various dimensions, occurred in a woman, aged thirty-eight, whose chief symptom was general

weakness and fatigue and whose bowels had moved regularly once a day. There were eighteen lesions, each larger than 6 cm. in diameter, and five lesions each smaller than 6 cm. in diameter. A specimen was not obtained in nineteen instances; these represented the inoperable lesions, with gross multiple metastatic extension, in which only exploration was done.

These specimens which were removed, were graded as follows: grade 1, five specimens; grade 2, seven; grade 3, five, and grade 4, six.

The *postoperative course* of this group of forty-two patients was as follows: died in the first three months, thirteen patients; died in the first year, nine; died in the second year, three; died in the third year, one; died in the fourth or fifth year, one; living at end of five years, ten, and not traced, five.

One of the patients, who had a carcinoma of the intestine removed in 1927, returned in October, 1934, without presenting signs of recurrence.

COMMENT

This report emphasizes again how one lesion in the abdomen can mimic another much more serious one. Is this the result of similar nerve supply or is it attributable to lack of fundamental knowledge of abdominal pathology? Certainly, most intestinal carcinomas exhibit symptoms which are directly referable to the intestine. This group represented only 6.7 per cent of the patients who were operated upon for carcinoma of the colon. So relatively high a percentage compels the observer to wonder how many other patients are going about harboring carcinoma, unwittingly.

It is noteworthy that of those lesions which were localized by roentgenologic study, nineteen were in the ascending colon. In this connection, it is interesting that, in nine cases, the symptoms were suggestive of disease of the gall bladder. The incidence of inoperability here varies little from that of the entire group of intestinal carcinomas. The number of five-year cures, too, is similar to that given in other reports. These appear as the only gratifying features.

It would seem, then, that even though the lesions may not have been diagnosed before operation, the symptoms pointing to intra-abdominal disease were such as to warrant exploration.

Portal Cirrhosis The Combined Medical and Surgical Management*

(With Report of an Instance)

By

HOWARD A. RUSK, M.D.

and

HAROLD G. NEWMAN, M.D.

ST. LOUIS, MISSOURI

OUR purpose in presenting this report is to outline the combined medical and surgical management of an instance of ascites and edema resulting from portal cirrhosis. It is of interest, that the patient previously had been treated by the commonly accepted methods without benefit. Nephritic diet, restricted fluids, saline, xanthine and mercurial diuretics all had been used without avail. Repeated abdominal paracentesis was necessary to make the patient's existence tolerable.

It was obvious that this patient required some effective measure of diuresis, and at the same time an ample diet in order to compensate for the enormous loss of body protein through the ascitic fluid. Such a method was recently outlined by Barker (1), in the treatment of certain types of nephroses and also in other types of chronic edema. This author pointed out that, in fluid retention, the sodium ion rather than the chloride radicle holds the water. He has shown experimentally, that the replacement of the sodium ion with potassium is followed by a marked diuresis. Dogs made edematous by reducing their serum proteins can be made to store or lose fluids at will by substituting the sodium and potassium salts in the diet.

Clinical success in Barker's treatment of edematous patients followed the giving of a high protein diet (150 gm.) with an acid ash residue and a low ratio of sodium to potassium. Potassium chloride was given in amounts varying from four to eight grams daily. The patient sprinkled from a salt shaker the amount necessary to make food palatable and took the balance of the daily dosage in water at night. Such a *regime* seemed practical in the management of portal cirrhosis, because it not only offered a method for sharp diuresis, but the diet also supplied adequate replacement of the protein lost in the ascitic fluid. The following case report gives the procedure in detail:

*From the Department of Medicine, St. Luke's Hospital, St. Louis. Submitted November 14, 1934.

CASE REPORT

A. K., a white male, ex-bartender, aged 67, was admitted to St. Luke's Hospital September 12, 1932, complaining of marked enlargement of the abdomen, swelling of the lower extremities and dyspnea. He had been treated elsewhere without success, for cardio-renal disease, and during the preceding nine months abdominal paracentesis had been performed eleven times; from twelve to fifteen liters of clear, amber fluid had been obtained at each tapping.

The patient gave a history of excessive use of whiskey for many years. He had noticed evening edema of the lower extremities for two or three years; this had been much worse for several months prior to admission. During this time the abdominal enlargement had also been increasing. He complained of frequent urination and nocturia, but his actual urinary output had been extremely small.

Physical examination disclosed an emaciated, elderly man with a greatly distended abdomen exhibiting a well marked fluid wave, pitting edema of both legs and ankles, and a typical "hepatic *facies*." The heart was normal to physical examination. Pulse 72. Blood pressure 106/76. The chest was negative except for occasional moist rales at both bases.

Laboratory findings: The urine showed a faint trace of albumin and many fine granular casts; N.P.N. 41 mg.; P.S.P. 10 per cent in two hours (the dye output was 40 per cent after diuresis became established); blood sugar 82 mg. per cent; blood chlorides 450; blood calcium 9.6; blood phosphorus 2.5; serum albumin 3.1 gm.; serum globulin 5.0; Wassermann negative; W.B.C. 11,000; R.B.C. 5,500,000; hemoglobin 67 per cent.

An *electrocardiogram* was normal, with left axis deviation; *X-ray examination* revealed a heart of normal size.

An *abdominal paracentesis* on the first day of admission yielded 13,500 c.c. of a sterile, clear, straw-colored fluid with a specific gravity of 1.020.

During the second twenty-four hours in the hospital the patient's fluid intake was 2600 c.c. and he eliminated 1000 c.c. of urine. On the third day after admission, he was placed on a high protein (150 gms.), salt-free diet, yielding an acid ash residue and was given 4 gms. of potassium chloride daily. After the first twenty-four hours his urine output balanced his fluid intake, but after several days of this *regime* he began to gain in weight from 250 to 300 gms. daily. The potassium chloride was then increased to 8 gms. daily and again diuresis increased. In spite of the increased dosage of potassium chloride, gradually the abdomen began to fill and it required paracentesis.

After thirteen days upon 8 grams daily dosage of potassium chloride, the patient showed definite signs of potassium intoxication, numbness of the extremities, nausea, headache and blurring of vision. The drug then was withheld for five days and the symptoms of intoxication cleared, but the urine output fell to 280 c.c. for 24 hours. The drug then was given in its original dose with a resultant mild diuretic effect. However, soon it became evident that more drastic measures were necessary. Dr. O. R. Sevin saw the patient in consultation and subsequent to a blood transfusion, he was transferred to the surgical service for omentopexy.

Operation: On October 21, 1932, under ethylene anesthesia, the abdomen was opened through a right rectus incision. There was a large amount of free fluid in the peritoneal sac. The liver was small, hard, nodular and gray in color. The spleen apparently was normal but adhesions were present from its lateral wall to the parietal peritoneum. The anterior surfaces of the spleen and the liver and the parietal peritoneum were scarified; the omentum then was sutured to the parietal peritoneum and to the anterior abdominal wall.

Post-operative course: The patient stood the operation well and had an uneventful post-operative recovery. During convalescence no efforts were made to treat him medically, his management being purely symptomatic and supportive. His intake and output of fluid balanced fairly well for a time, but after two weeks the urinary output again fell far short of the intake. The abdomen was filling slowly. Seventeen days after operation again he was given a high protein diet and 4 grams of potassium chloride daily. In one week the dose of potassium chloride was increased to 6 grams; this was well tolerated. On the 25th day after the operation, *paracentesis* was performed. When the trocar was introduced, there was a gush of air and 3600 c.c. of frothy asitic fluid was withdrawn. Following this, although the urinary output failed to equal the fluid intake, the abdomen remained flat and the patient became generally hydrated. He gained strength rapidly and felt much better generally. On November 11th, thirty-two days after operation, he was discharged, a high protein diet being prescribed with six grams of potassium chloride daily. Observation at frequent intervals in the out-patient Clinic showed that while the patient's weight increased slightly, his abdominal measurements remained constant.

On March 9, 1933, five months after the operation, he was given a regular diet with no limitation of sodium chloride. He was asked to ingest this diet for a week and then return for observation. He returned voluntarily in four days, stating that he was quite uncomfortable. His urinary output was scant and he had gained seven pounds in weight. He was immediately returned to his old regime and continued reasonably comfortable without paracentesis, the abdomen remaining soft.

Repeated albumin-globulin estimation of the serum throughout the illness and convalescence showed constantly a reversal of the normal ratio. The last reading on February 3, 1933, was serum albumin 3.8, serum globulin 5.0, which is practically the same ratio as that found on admission and on subsequent examinations.

The patient continued quite well until July 18, 1933, when he became semi-comatose, developed signs of cardio-renal failure; this condition gradually progressed, and he died on August 14, 1933.

AUTOPSY REPORT

Pathological Diagnoses: (Dr. L. S. N. Walsh).

1. Cirrhosis of the liver, nodular; 2. Ascites, slight; 3. Laparotomy scar (Talma-Morison) with loose vascular adhesions binding together practically all the viscera in the upper abdomen; 4. Hydrothorax, bilateral, slight; 5. Chronic passive congestion of lungs; 6. Hemorrhagic erosions and pigmentation of gastric mucosa; 7. Hypertrophy of left ventricle; 8. Chronic fibrous myocarditis; 9. Chronic diffuse nephritis; 10. Broncho-pneumonia; 11. Chronic peritonitis with adhesions around cecum and ascending colon; 12. Chronic fibrous perisplenitis with adhesion to the diaphragm; 13. Chronic fibrous pleurisy with adhesions; 14. Pulmonary emphysema; 15. Inguinal hernia; 16. Emaciation.

DISCUSSION

A review of the literature on edema reveals the fact that considerable controversy still exists regarding its mechanism of production. Many factors have been shown to be involved in base excretion and water balance, and in any given case probably several factors are at work, and may be responsible for the storage of fluid.

Youmans (2) calls attention to epidemics of *nutritional edema* due to inadequate diet. Such cases studied at Vanderbilt Hospital showed typical edema of the feet and legs with involvement of the hands and face in some subjects. This edema was ascribed to hypoproteinemia from inadequate protein intake. When an adequate diet was given, cure quickly followed. In Youmans'

cases, the total serum protein was found normal or only slightly diminished, but all patients were low in serum albumin. The serum globulin, however, was normal or above in most cases.

This finding corresponds to our determinations. Repeated analyses gave a ratio of 2-1 globulin to albumin with total protein normal or slightly low. Youmans believes edema probably depends on the balance of force between the capillary pressure tending to force fluid out of the vessels and the osmotic pressure of the plasma tending to hold the fluid in.

Trumper and Cantarow (3) state that the normal total plasma protein concentration is 6-8 gm. per 100 c.c. Of this 4.5-5.5 gm. is albumin and 1.5-3.0 gm. globulin. The ratio should be, albumin 1.5-2.5 to 1.0 of globulin, this being just the reverse of the ratio constantly shown in our patient. They further state that plasma proteins do not serve as a source of nutrition to the tissues. Their chief function is to exert colloid osmotic pressure, and in that capacity they play an important part in maintaining normal distribution of water between the blood and tissues.

Because of the fairly high degree of diffusibility of the crystalloids, the concentrations of these substances in plasma and tissue fluids practically are identical. Therefore, in the resting state, the crystalloid osmotic pressure of plasma is balanced by that of the tissue fluids. Because of differences in protein content of plasma and tissue fluids, the colloid osmotic pressure of the plasma tends to direct the flow from the tissues to the blood stream. Trumper and Cantarow further state that any marked decrease in albumin usually is followed by an increase in globulin. Probably as an attempt to compensate for the primary deficiency. As a consequence, the albumin-globulin ratio is decreased or actually reversed. The resulting diminution in colloid osmotic pressure decreases the ability of the plasma to hold water. The globulin molecule being larger is unable to exert sufficient osmotic "push" to compensate for the loss of albumin, and then edema results. The above cited investigators state that, according to Iversen, each gram of albumin in 100 c.c. serum exerts an osmotic pressure of 7.54 cm. of water as compared with 1.95 cm. of water per gram of globulin.

Barker (1), who previously has been quoted, calls attention to the effect of the motor power of the heart, of the quality of the blood and of the renal function in edema. Herrman, Stone, Schwab and Bondurant (4), in a paper dealing primarily with the localization of the action of various diuretics, call attention to the importance of edema clinically. They too, state that recent work tends to show that the part played by the serum proteins may be more important than is that of the shift in the electrolytes.

Hartmann *et al* (5) stressed the relationship between the reduction in concentration of plasma protein and edema of non-cardiac origin. These observers state that, in severe instances, the loss of plasma proteins through the kidneys exceeds the possible protein intake and that transfused protein may remain in the circulation for too short a time to be of practical service. They report the successful use of acacia solutions, intravenously, in amounts sufficient to restore the oncotic pressure of the plasma to a point above the edema force.

Omentopexy seems to have been devised following the frequent observation that repeated abdominal paracentesis often gave permanent relief. This was thought to be due to the return of portal blood to the general circulation through vascularization of adhesions produced by the trauma. Talma usually is credited with devising the operation in 1889. Van der Menke following his technic, performed the first operation but with fatal results. In 1891, Lens operated successfully; the patient lived six months. In 1895, Morison performed the first really successful operation; the patient lived comfortably for many years. Since that time the literature is fairly voluminous concerning the more or less successful use of the Talma operation or its modifications.

The literature records much controversy concerning the mechanism of production of ascites. Binnie (6) states that ascites is due to several causes. He states that the common belief that ascites results from a "damming up" of the portal system and the consequent back pressure is contested by Rolleston and Turner. They claim that ascites does not occur early in portal cirrhosis, at a time when the pressure is highest. Moreover, they point out that ligation of the portal vein does not produce it. Rolleston and Turner think that ascites is the result of a toxemia rather than representing mechanical extravasation from back pressure. They further claim that any benefit following operation is produced by allowing less blood to flow through the liver, thus giving the liver a better opportunity to detoxify what does pass through. New adhesions, moreover, allow a better arterial supply to reach the liver, thus improving the nutrition of the cells and favoring compensatory hypertrophy. Binnie condemns Eck's fistula as being too toxic in its effects for the human organism to stand successfully.

Horsley (7) states that the Talma operation "sidetracks" the blood stream and thus relieves tension on the portal circulation. He believes that this diminution of pressure often is followed by decreased ascites. The Talma-Morison operation produces an anastomosis between the vessels of the portal circulation and those of the general circulation and thus relieves the former without admitting to the general circulation more than a small portion of the material absorbed from the intestines.

Osler made the statement that repeated paracentesis removes so much of the nutrient fluid, that once tapping is started, fourteen weeks then is the average life expectancy. Added to this, of

course, is the tremendous danger of infection from contamination in repeated paracenteses; moreover, the prognosis in portal cirrhosis of itself always is grave.

COMMENT

Decompensated cirrhosis of the liver presents a complicated problem to both internist and surgeon. Surgery only can be of benefit from a purely mechanical standpoint. With the tremendous protein loss, conservation of the body proteins becomes absolutely essential. It may be necessary to resort to blood transfusion or the exhibition, intravenously of acacia suspensions as temporary expedients, but only a tremendous, utilizable protein intake, plus a rational diuretic regime can be of permanent benefit, after the mechanical factor has been corrected to the *optimum*.

Such a *regime* best was accomplished in our subject by a diet containing 150 gms. of protein, with an acid-ash residue, low in sodium and high in potassium. Under such *regime*, our patient lived comfortably for a year, with his cirrhosis entirely compensated.

The unusual observations in this patient were the diuresis and the maintenance of the water balance, with a constant inversion of the albumen-globulin ratio. From such one only can conclude that the diuresis was due to the substitution of potassium for sodium and the acid-ash residue in the diet.

We are reporting the management of this isolated case, not because we feel that it is conclusive, but as an example of the combined chemical, physical and mechanical approach to a complex medico-surgical problem.

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ABSTRACTS

EASTON, E. R., AND WATSON, W. J.

Analysis of 100 Complicated Cases of Acute Appendicitis. Primary Cecostomy or Enterostomy as a Life Saving Procedure. Surgery, Gynecology and Obstetrics. Vol. LVIII, No. 4, April, 1934, pp. 762-767.

The authors cite statistics showing that the death rate from appendicitis has increased from 9.7 per 100,000 population in 1900 to 15.2 per 100,000 in 1929. The major causes are (1) indiscriminate use of purgatives by the lay public, (2) delayed operation, (3) imperfections in operative technique.

Cases of long standing appendicitis with abscess formation, and diffuse peritonitis treated by primary enterostomy with recovery are cited. The advantages of primary enterostomy, or cecostomy, are (1) that it forestalls the onset of postoperative ileus, (2) that it prevents obstruction from adhesions by keeping the intestines in motion and allowing prompt escape of gas and fluid, (3) that the wound heals almost as promptly as the appendiceal wound and causes no additional strain upon the patient.

Postoperative ileus should be diagnosed early and treated promptly before a profound toxemia supervenes. Moynihan believes that 15 out of 20 enterostomies are performed too late. In the authors' series the cases selected for cecostomy or enterostomy were those which, when the abdomen was opened, revealed a dull, lusterless gut distended with gaseous and liquid material, and with plastic adhesions between the distended coils of bowel.

The procedure recommended for cecostomy is as follows: A No. 20 French catheter in which several additional holes have been made is stretched and grooved with a scalpel to form a ring about 8 inches from its rounded tip. A stab wound is made just lateral to the operative wound just mesial and inferior to the anterior superior iliac spine about one inch above Poupart's ligament, and parallel to it. The lateral wall of the cecum is brought out through this opening in the abdominal wall. A purse string suture of No. 0 chromic is placed in the wall of the cecum. A small puncture wound is then made in the center of this purse string area. The catheter is passed through the puncture wound in the cecum, and carefully insinuated through the ileocecal valve. The purse string is drawn taut, and tied securely at the grooved ring. This area is then inverted with one or two additional purse strings of the No. 0 chromic. The portion of the cecum containing the catheter is then pushed back into the abdomen, and caught with a catgut suture at each end of the peritoneal incision so as to hold it firmly against the abdominal wall. A silk worm suture is then passed through both edges of the stab wound and the catheter to hold it in place. Drainage and closure of the appendiceal wound are then concluded in the usual manner. This technique is recommended because of the short period of its subsequent closure; drainage of fecal matter ceases within a week, and the wound is healed within three weeks.

In the case of a jejunostomy, or ileostomy, any method modified after the Witzel method is satisfactory. In such, a No. 14 catheter will drain the bowel "as well as a garden hose" according to Wangensteen.

In roentgen diagnosis it must be shown first: that a portion of the cardiac end of the stomach must be shown to stay above the level of the diaphragm, and second: that the esophagus must be shown to be too short to reach below the diaphragm.

The characteristic sign of the first point is the presence of longitudinal rugae markings in the cardiac portion of the stomach above the diaphragm. The second point is established by visualizing the entire length of the esophagus and by different views to demonstrate that it is not tortuous or angulated but simply short. At esophagoscopy evidences of chronic esophagitis and some dilatation of the thoracic esophagus were found.

Ulceration involving the funnel-like opening was observed in eight of the fourteen cases. In eight cases specimens of tissue removed from the suspected thoracic stomach showed gastric tissue. In treatment, cases with ulceration were given alkalies and bismuth subnitrate. Applications of ten per cent silver nitrate topically gave some relief. Dilatation of stenotic area may offer relief.

Francis D. Murphy.

WALTERS, WALTMAN.

The Treatment of Extensive Malignant Lesions of the Stomach. J. A. M. A., 103:1345 (November 3), 1934.

All malignant gastric lesions should be regarded as extensive, because even the very small lesion may be highly malignant and produce glandular involvement.

The large malignant lesions of the stomach are usually localized in the stomach and are frequently of low degree of malignancy and it is quite necessary, therefore, that they must be removed. Fluoroscopic and roentgenographic examination may seem to indicate that the lesion was wholly inoperable or doubtfully operable, yet in more than one-half of this group of cases the lesions were removed successfully.

An increasing number of extensive malignant lesions of the stomach are being removed today due to the fact, it seems, that no matter how extensive the lesion of the stomach may be, abdominal exploration is done, providing the patient's general condition permits it and remote metastasis is not demonstrable.

Patients in the sixth, seventh or even eighth decades of life stand operation well. The general condition of the patient and not the age is the factor in the surgical mortality.

Technical procedures assisting in removal of extensive gastric lesions are to approach the stomach through a left rectus incision, to begin resection by dividing the duodenum below the pylorus, and to complete the posterior portion of the gastrojejunal anastomosis to the posterior wall of the stomach high above the lesion before the latter is removed. This enables a larger segment of the stomach to be removed. A temporary jejunal stoma for feeding has permitted administration of nourishment into the intestinal canal during the postoperative period in which healing of the anastomosis is taking place. If further progress is to be made in securing a larger proportion of cures in cases of carcinoma of the stomach, every effort must be made to recognize the presence of malignant gastric lesions in their earlier stages, and in this roentgenologic examination of the stomach is of the greatest assistance.

Francis D. Murphy, Milwaukee, Wisconsin.

JOHNSON, LLOYD, B., AND RENNER, GEORGE, JR.

Peptic Ulcer of Meckel's Diverticulum. A Report of Two Cases and a Review of the Literature. S., G. and O., Vol. LIX, No. 2, August, 1934; pp. 198-209.

The clinical picture of peptic ulcer of Meckel's diverticulum is comparatively new. Deetz first described it in 1907. Since that time many cases have been reported; the greater number since 1920.

The authors review 78 cases found in the literature, and report two cases of their own. They are divided into three groups. Group I includes 48 cases of definite ulcer in which gastric, duodenal or pancreatic mucosa were definitely demonstrated. Group II includes 14 cases, which were quite probably peptic ulcers but were not proved to be so microscopically. Group III includes 16 cases in which definite ulcers were not demonstrated.

There is usually a single ulcer located at the base of the diverticulum at the junction of the gastric and ileac mucosa, and extending into the ileac rather than the gastric mucosa. Occasionally multiple ulcerations are present.

The condition is much more common in the male; of the definite ulcer cases 49 were in males, 9 in females, and in 4 cases the sex was not stated. Although the age varied from five months to forty-five years, the ulcers are predominately in infants and children.

Intestinal hemorrhage is the most constant symptom. The bloody stool may vary in color from bright red to black; it is usually dark red in color. Collapse, or a state of extreme weakness and anaemia, may result from repeated hemorrhages. If perforation does not occur the individual is likely to recover, and then after a lapse of weeks, months or years suffer a recurrence of the hemorrhages.

Next to hemorrhage the most frequent complication is perforation, in which case the clinical picture is one of an acute surgical abdomen. In the differential diagnosis the blood dyscrasias, intussusception and chronic duodenal ulcer are easily ruled out by a complete blood count, absence of mucoid stools and no history of previous digestive disturbance, respectively. Rectal examination excludes rectal polypi.

The treatment of this condition is obviously surgical. Blood transfusions are frequently necessary before operation is performed if the patient is very anaemic. It should be kept in mind that while the patient is weakened by loss of large amounts of blood perforation is most apt to occur. A number of very anaemic patients have developed acute perforation while under observation. In most cases the diverticulum can be excised with a narrow cuff of intestinal wall; in some a resection of a segment of the ileum is necessary. The surgical record in the treatment of this condition is very good in all cases excepting those with perforation and diffuse peritonitis.

The article is accompanied by three tables giving a brief record of each case reviewed, and a detailed record of the cases reported, several photomicrographs, and a large bibliography.

Nelson M. Percy, Chicago, Illinois.

LONGACRE, J. J.

Mesentericoparietal Hernia (Duodenal Hernias of Treitz). S., G. & O., Vol. LIX, No. 2, August, 1934; pp. 165-176.

The author reviews most of the theories concerning the formation of "the exceptionally rare case of a peritoneal hernial sac holding all of the small intestine". Such hernias which are perhaps more widely known as "Duodenal Hernias of Treitz" are believed by most authors to arise as post-fetal developments. Treitz believed that any of the small peritoneal fossae about the duodenum might be deepened and widened to form the hernial sac by the pressure and peristaltic movements of the intestines. Others have thought that elevations of the peritoneum over blood vessels or adhesions or persistence of the ventral mesentery might exert forces which resulted in the hernia. In spite of the finding of these hernias in new-born babies, and infants, the possibility of their interpretation on an embryological basis was never considered until the relatively recent works of Andrews and others. In 1923 Andrews advanced the view that the condition was a congenital anomaly due to the imprisonment of the small intestine beneath the mesentery of the colon. He declared that "the view that these small peritoneal pouches of which there are hundreds scattered about the abdomen are the origin of these hernias is absurd and grotesque". In support of his views he pointed out some pertinent facts, viz:

1. Differential pressure within the abdomen is completely lacking.
2. Herniated viscera are never anything but small bowel. The presence of omentum has never been noted.
3. In all but a very small minority of the cases reported, the degree of herniation has been total or subtotal.
4. Vogt reported a case in which such a hernia was complete in a new born. In the German literature these hernias were first termed "mesentericoparietal". Hertzler is extremely doubtful that the gut ever pushes its way into any of the various peritoneal fossae, stating that pressure in the potential sac is equal to that in the abdomen. He feels that it is

far more probable that in the rotation of the colon and descent of the caecum with the fusion of their mesenteries to the posterior abdominal wall, part or all of the small intestines are left in a peritoneal pocket.

In order to understand the production of these hernias it is necessary to grasp the basic embryological changes in the development of the intestinal tract. According to Andrews, "if no rotation of the umbilical loop of the mid gut occurs, or if rotation occurs through an angle of 180 degrees in the reverse direction, the caecum would then come to lie in the lower abdomen on the right side. As the colon gains in length and the caecum seeks its normal primitive position in the left upper quadrant the small bowel is caught beneath the mesentery of the colon" preventing its fusion with the posterior abdominal wall. The key to the solution of the mode of production of these hernias lies in the careful dissection of the inferior mesenteric artery and vein and their relation to the hernial sac. Garber first recognized that point.

The author describes in detail two cases of mesentericoparietal hernia in each of which the inferior mesenteric artery or vein or several of its branches were found in the anterior wall of the hernial sac, the remainder of that group of vessels being at the superior fused margin. In each case the caecum and redundant colon were attached to the opening of the hernial sac. Both of the author's cases may be classified as total mesentericoparietal hernias, there being, in each case, a short segment of ileum extending from the caecum to the sac. Significantly, too, normal paraduodenal pouches were found in both cases.

To date, 140 cases of such hernias have been reported; only 5 have been correctly diagnosed before operation. According to Garber the history of periodic distention of the abdomen associated with a sense of heaviness when coupled with the finding of a tympanitic elastic tumor in the left hypochondrium is very suggestive of a partially obstructed duodenal hernia.

Treatment of such hernias depends on the status of affairs found at operation. Strangulation may be relieved by widening the opening of the sac and resection of as much of the sac as the position of the blood vessels will allow. The high mortality in the treatment of such conditions can be reduced only by a more thorough grasp on the part of the operating surgeon of the anatomical anomalies at hand.

The author concludes that in the light of the new embryological concepts the anatomical details of the cases presented indicate that the so-called "duodenal hernias of Treitz" are true congenital anomalies produced by the incarceration of the small intestine behind the mesentery of the colon. In view of the mechanism of production of these hernias the term "mesentericoparietal" hernias has been applied to them.

Eight figures illustrating the cases reported, the mechanism of normal rotation of the intestinal tract, and the particular mechanism of rotation in each of the cases reported, accompany the article.

Nelson M. Percy, Chicago, Illinois.

McEVERS, A. E.

Conservative Treatment of Acute Duodenal Fistula. Surgery, Gynecology and Obstetrics. Vol. LVIII, No. 4, April, 1934, pp. 786-790.

The author discussing the conservative treatment of acute duodenal fistula states that the objectives of the treatment are:

1. Chemical, nutritional and fluid loss replacement.
2. Nutritional maintenance.
3. To buffer the action of the digestive enzymes contained in the discharge from the fistula.
4. Protection of the skin by applications to prevent erosion.
5. Strapping of the discharge sinus to lessen the loss of duodenal secretion.

It has been established that chemical and fluid loss can be replaced and maintained. Nutrition can be maintained by the administration of salt and glucose solutions, hypodermically and intravenously, and by feedings through a duodenal or jejunostomy tube. The corrosive action of the discharge from the sinus is due chiefly to the pancreatic component. It has been suggested that large amounts of water by mouth, and flushings of the tract, may dilute the secretion, and diminish its corrosive properties. Acidulation of the discharge with tenth-normal hydrochloric acid has been suggested. Other materials to fix, or inactivate, the enzymes have been used. Suction to carry away the secretion could be used advantageously, if it were not for the difficulty of its application. Exposure of the wound and sinus opening to the actinic rays of a 750 watt carbon bulb for two to four hours twice daily is helpful.

Various substances have been used to buffer the action of the digestive enzymes present. Whole milk thickened by the use of acidophilus placed locally in the wound and fistula with tenth-normal hydrochloric acid applied by means of a catheter has been used. The author in the case which he reports attempted to buffer the tryptic action of the secretions before they entered the fistulous tract by using reliquefied "recolac". Recolac was selected because of the simplicity of its preparation; boiled milk, or any reliquefied milk concentrate could be used with the same result.

Under sterile conditions recolac is dissolved in water, one ounce of recolac to seven ounces of water.

Six ounces of this preparation are given by mouth every two hours for eight times in twenty-four hours, a total of forty-eight ounces with a caloric value of 912 calories.

Eight ounces are given every 2 hours for 8 times in 24 hours by a jejunostomy tube, a total of 64 ounces with a caloric value of 1,216 calories.

Chloride and sodium ions are replaced by intravenous and subcutaneous administrations. By means of the jejunostomy tube additional materials may be administered; glucose or saline in concentrated solution, and lubricants to aid in elimination may be given.

Tight strapping of the fistulous opening of the abdominal wall, providing there is no pus in the discharge, should be carefully applied and maintained. The skin may be protected with zinc oxide ointment of kaolin powder.

The author advocates this treatment when the first signs of duodenal secretion are seen in the wound; one should not wait until the fistula is well developed.

By way of anticipatory treatment he suggests that a well functioning jejunostomy be established at the time of the primary operation, and that no drainage be employed. If drainage is necessary, soft rubber, of the Penrose type without gauze, through a stab wound in the right flank, should be used. It should not be placed in contact with any suture line in the duodenum.

The author recommends this treatment for acute duodeno-cutaneous fistulae only; it is not intended for duodeno-colic, or other internal fistulae. He feels that the buffer solution of milk with modification, or reliquefied milk concentrate, given at frequent intervals by mouth, reduces the corrosiveness of the duodenal secretion sufficiently, that flushings of the tract, or the administration of hydrochloric, or other acids, is unnecessary.

One case of acute duodeno-cutaneous fistula treated as outlined above is reported.

Nelson M. Percy.

ARNHEIM, E. E., AND NEUHOF, HAROLD.

A Lowered Mortality in Acute Appendicitis, and the Basis Therefor. S., G. and O., Vol. LIX, No. 2, August, 1934, pp. 189-193.

The authors report from the surgical service of one of them at the Mount Sinai Hospital in New York the mortality statistics for all cases of acute appendicitis over two "three-year" periods; the first period from 1928 to 1930 inclusive, the second from 1931 to 1933 inclusive. During the first three-year period the mortality from all forms of appendicitis was 8.2 per cent. In 1930 the

authors made several changes in the management of certain cases with the result that in the second three-year period the mortality rate was 2.8 per cent. More than 100 cases of appendicitis of the milder forms in the treatment of which there was no mortality were not included because the general mortality rate would be so lowered that the results in the significant groups might be glossed over. In the groups of cases of acute appendicitis with abscess, and acute appendicitis with localized peritonitis, the greatest improvement in mortality rate was made; the mortality rate in the former group was reduced from 21.2 per cent to 6.4 per cent in the two periods studied, while in the latter group the mortality was reduced from 22.2 per cent to .0 *(nil)* (zero) during the same periods.

In the first three-year period autopsies showed that suppuration was the chief, if not the sole cause of death in all fatal cases. This suppuration which occurred after operation suggested to the authors that there must be something fundamentally wrong in the management of such cases. The problem was attacked anew from several angles: individualization of cases, indications for operation, operative technique, and general management.

A very carefully taken history is the most important factor in making the diagnosis of acute appendicitis. A localized point of tenderness is accepted as a guide to the location of the appendix. Occasionally a left-sided abdominal puncture is done to determine the presence or absence of peritonitis, or the degree of peritonitis if it is present.

All cases having a short history (within twenty-four hours) are operated upon immediately. Many cases of from 36 to 48 hours duration are operated on immediately. Frequently those in the second or third day of the attack are treated with rest in bed, opiates sufficient for rest and quiet, and fluids. An intravenous drip of 5 per cent glucose in saline is used in such cases. The temperature and pulse rate usually drop with rest in bed. Young children and infants are operated upon promptly because of the difficulty of determining the extent of the lesion, and an apparently smaller likelihood of walling off of the infection. Immediate operation is contraindicated in most cases of appendiceal abscess. With bed rest, intravenous fluids, and a light liquid diet their general condition improves.

Critically ill patients with diffuse peritonitis are given bed rest, morphin, intravenous glucose in normal saline, and are under observation. After several hours marked improvement is apparent.

In all cases placed on preoperative intravenous therapy the slow drip is continued throughout the operation, and for some hours or days afterward.

Avertin alone or combined with nitrous oxide and ether are used in most cases. Spinal anaesthesia is reserved for obese patients who are not gravely ill.

Adequate exposure through an incision over the point of maximum tenderness (or over the mass if one is present) is advocated. Vigorous retraction is to be avoided.

After the abdomen has been opened suction is kept at hand for removal of pus, and infected fluid, in the operative field. The small intestines are packed off with moist pads or packings. The appendix is delivered from base to tip using Allis forceps. All contaminated instruments are at once discarded. When a mass is present an abscess is presumed to exist, and preparations to aspirate its contents are made. Abscess cavities are explored to their limits.

Drainage by packing with iodoform gauze is employed in all abscess cases, and in other cases in which there has been much purulent material. If the appendix was removed from a retro-cecal position, drainage is employed more often than when it is found in other positions. Drainage by tubes is not employed. Contaminated instruments and gloves are discarded after the packing has been put in place. The wound is closed in layers, but not tightly about the drains.

Postoperatively the drains are not disturbed until they are loosened by the discharge. Their gradual shortening is usually begun about a week after operation. Frequently the wound is lightly repacked with gauze after the first pack has been removed. The indwelling Levin tube and colonic irrigations are used as commonly advocated. The administration of glucose 5 per cent in saline is continued as before. Opiates are used freely. Cathartics are rarely used.

The authors are prone to consider that any patient who is not doing well after operation is suffering from infection related to the operative field. A close watch for intra-abdominal complications is maintained in such cases; left-sided abdominal puncture to determine the status of the general peritoneal cavity is frequently used in such cases.

In the experience of the authors the mortality rate in the severer forms of acute appendicitis, excepting those cases with diffuse peritonitis, has been greatly lowered by following the plan of management outlined.

Nelson M. Percy, Chicago, Illinois.

GATELIER, JEAN *(Paris)*, AND WEISS, ALFRED.

Pathology and Treatment of Proctitis with Proliferation and Stenosis. Jour. de Chirurgie, Paris, Octobre, 1934.

This extensive work can be summarized as follows:

(1) The proctitis with proliferation and stenosis constitutes but one of the clinical aspects of a more general affection essentially characterized by a process of lymphangitis and liable to invade respectively or simultaneously the various lymphatic systems of the perineum, the anorectal region, the genital organs, the inguinal regions or the lower abdominal quadrants; (2) In the majority of cases this "parade-nolymphangitis" is due to the virus of the "Nicholas-Favre Disease" as the authors have well brought forth in their report with histological, biological and clinical proofs; (3) Among the various etiologic factors previously held responsible for this disease, syphilis, gonnorhea, and mycosis have been clearly eliminated. However, a doubt remains relative to the possibility of a tuberculous origin in two observations where the Koch bacillus was identified, thus explaining the nature of certain inflammatory stenoses of the rectum. Anyway, this contingency is exceptional; (4) The examination of *139 cases* of inflammatory stenosis of the rectum treated by various surgical methods, and by different surgeons, cases well followed up during many years, has proved the actual failure of the surgical processes of amputation. Relapses are a rule except for rare cases; (5) A study of the mechanism and of the pathologic reasons of those relapses has led the authors to consider the *peri-rectitis* as the essential factor of those surgical failures. Even the high and extensive rectal amputations, the sections up to healthy mucosa are not sufficient to obtain a definite cure; (6) The characters of this perirectitis, as distinguished by the authors, are those of a sclerogenous disease invading all the perirectal, perineal, ischio-rectal and sub-peritoneal regions, thus causing a fibrous mass constantly progressing into the neighbouring tissues; (7) Understood from this standpoint the amputation of an inflammatory stenosis of the rectum, even of a proctitis with proliferation under progress, can not be a resection of the diseased mucosa or of a mucous or submucous stenosis, or of a parietal proctitis. The diffuse sclerosis deprived of all limits or planes of cleavage, cannot be operated upon with disregard of the lymphangitis which carries infection; thus, limiting operation to apparently sound tissues is not adequate because in such seemingly sound tissues, one may have infected lymphatics; (8) Because of the post-operative results, the author actually advises the conservative or medical treatment associated, in certain cases, with an iliac stoma. These palliative methods are, however, uncalled for when the specific treatment of definite etiologic factors permits a cure of the proctitis with its proliferation and stenosis by radical measures. Surgical treatment is most efficacious when one deals with tissues which are true scar tissues and which contain neither elements of the original rectal structure or infecting organisms. Jean R. A. Le Sage, Montreal, Canada.

SECTION VIII—*Editorial*

The editorial contributions published in this Journal represent only the opinions of their writers. Such being the case, this Journal or the American Association is in no way responsible for editorial expressions.

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

ABSTRACTS OF MEDICAL LITERATURE

One of the worth-while and distinctive features of the Journal lies in the number and quality of abstracts of articles which have appeared in periodicals other than this publication.

Particularly has appreciation been recorded in respect to the Journal's printing abstracts at the ends of its several sections instead of having them appear in an unrelated mass "somewhere towards the back cover", as is customary with many magazines. One cannot question the added value and significance when abstracts are available immediately following clinical and investigative studies in medicine, physiology, therapeutics, surgery, etc.

Evidently, to many of our contributors, abstracting proves to be a task more formidable than that of writing original articles. While, at present, there is such an accumulation of manuscripts that the selection for publication of those which are most likely to prove of value and interest to our readers, has become a perplexing editorial problem, yet, often enough, the supply of suitable abstracts is meagre: not that one has available no abstracts, but, it is not to be denied that on occasions, such as have been submitted do not represent material up to the standard required.

Many months past, to individual members of the Editorial Council, lists of leading medical publications were assigned for abstracting. Some Council members have been most faithful in performing their tasks: others have done little or nothing. This ought not to be: the labor should be shared equally by all those who form the Council. It is of interest to observe that from a surgeon recognized as one of this country's very busiest major operators, regularly have come large collections of abstracts.

All worth-while medical men are busy. Even in these days of economic puzzlement and stringency, the rightly-constituted physician keeps occupied. To some, opportunities for catering to hobbies are afforded; a number find pleasure and profit in rearranging the routines of their offices, of catching up on filing, of reviewing groups of cases which hold greater than ordinary interest, of manuscript or book writing, of testing new methods of procedure or of working with recently marketed and unique apparatus. Certain doctors steep themselves in what one might term "extracurricular" reading—general, science, the drama, music, philosophy, art (one whom we know well has experienced a happy year in collecting, reading and classifying books dealing with the "History of Dancing" and the various ramifications which become manifest when such a fascinating subject is explored), astronomy, polar exploration, medical history. To those physicians possessed of equanimity—and sufficient shillings stored safely away to detour the wolf from their doors—the past three years of business depression and thinly populated consulting rooms, have proved a boon: whereas previously these men had been so held to the treadmill of practice that what was going on in the world about them was an intellectual Sahara, the "depression years" have given opportunity for "playing hookey" into fields long forbidden. To physicians in mid-life this mental and psychic vacation from their life's work gladly has been welcomed. When the "new deal" again straps tightly about them their professional harness, the delights and knowledge acquired during the enforced "Sabbatical years" will result in their being more able as doctors because they have become more human as men.

It is to be hoped that in the hours available for flight from the demands of their craft, a larger proportion of the Editorial Council than now is computable, will arm itself with pencil and pad and, as they browse amongst the more than one hundred periodicals devoted to recording medical progress, they will abstract for this Journal those articles which mark advances in our art and our practices. A half hour a week just before turning in of a night not alone will bring pabulum—probably otherwise inaccessible—to our readers, but the satisfaction coming from a task well performed may prove a potent anti-insomnia remedy. But, even though the hour be late, take a moment to sign the abstracts! Not infrequently that is not done: in those circumstances, we are quite as greatly puzzled as is disappointed he who worked and yet later failed to find the results of his efforts printed.

Abstracting must be done when the "mood is on" and then as Goethe has it:

"Gebraucht der zeit:
Sie geht so schnell von hinnen!"

F. S.

INTRODUCING
FRED JENNER HODGES

To the Roentgenological Section of the Editorial Council, the Journal and its readers, we feel sure, welcome Dr. Hodges, Director of the Divi-

sion of Actinology at the University of Michigan, Ann Arbor.

After securing the degree of Bachelor of Science at the University of Wisconsin (1917), Dr. Hodges earned his Doctorate in Medicine at Washington University, St. Louis (1919). From 1919 to 1920, he was Resident Pathologist at Barnes Hospital in the same city. A year overseas with the American Red Cross broadened Dr. Hodges' outlook and experience and he returned to take up the duties of Instructor in the Department of Physiology at the University of Wisconsin. This position was held until 1924 when Dr. Hodges became Roentgenologist to St. Mary's Hospital at Madison, Wisconsin, and Instructor and Lecturer in Roentgenology at Wisconsin University. Upon the demise of Dr. Preston Hickey in 1931, eminent pioneer in Actinology, Dr. Hodges was called to the University of Michigan to serve as Professor of Roentgenology and Chief of the Department at the University Hospital.

Under Dr. Hodges' direction, extensive alterations and additions were made to the Roentgenological Department at the University so that at present it is regarded as one of the outstanding institutions of its kind throughout the world—not alone in equipment and in its unique arrangements for the clinical study of an enormous group of patients, but in respect facilities for undergraduate teaching and research. It has been claimed that no Roentgenologist can consider his training as being completed unless he has visited the Roentgenological Department at the University of Michigan Hospital.

Our readers can look forward to timely and valuable contributions to the Journal from Dr. Hodges and his Associates.

F. S.

PROFESSOR BOLDYREFF AND THE MAY, 1933, SESSION OF THE AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION

December 5, 1934.

To the Editor:

I should appreciate if you found possible to publish this letter in the Journal in order to clear up a few misunderstandings among the readers.

My report relating to diabetes and its management, given at the 37th Annual Meeting of the American Gastro-Enterological Association was read by another person. I was absent because of sickness and could not participate in the discussion. The slides which amplified my statements were not shown. Therefore, some people have incorrectly understood my data. For instance, Dr. B. B. Crohn believes that I find increased pancreatic secretion in diabetes mellitus whereas I insist on quite the opposite (as seen in my report, viz., this Journal, September, 1934, p. 453) in complete accordance with the observations of Dr. Crohn and other people whom he mentions. There is a misprint in his words, probably this should read "hyponormal".

Appreciating your courtesy and trusting that those of your readers to whom my contribution may be not clear will address their enquiries directly to me, I am

Sincerely yours,

W. N. Boldyreff, Battle Creek, Michigan.

ABSTRACTS

WILKIE, D. P. D.

Section VII. Surgery of Lower Colon and Rectum. Cancer of the Colon. Its Surgical Treatment. Lancet, 226:65, 1934.

Wilkie makes the positive statement that radiotherapy has no curative value in cancer of the hollow viscera of the abdomen; operation offers the only hope. Cecostomy, followed by extirpation of the growth after a delay of several weeks, is advocated when the patient has developed acute obstruction.

Resection is preceded by injections of vaccines of *bacillus coli* and by *streptococcus* eight, three days pre-operatively; the evening before operation nucleinate of soda intramuscularly is given to induce leucocytosis. A 15 per cent mortality is reported in 101 cases.

Curtice Rosser (Dallas, Tex.).

DEVINE, H. B.

Rectosigmoid and Sigmoid Surgery. Australian and New Zealand J. Surg., 3:211, 1934.

Because of mortality from leakage and soiling when primary resection and anastomosis is performed on the left colon, Devine advocates routine temporary transverse colostomy as a first step, believing that this procedure permits an aseptic second stage operation.

Curtice Rosser (Dallas, Tex.).

ROWNTREE, L. G.; CLARK, J. H.; HANSON, A. M., AND STEINBERG, ARTHUR.

The Biologic Effects of Thymus Extract (Hanson). Volume 103, No. 19, Page 1425; November 10, 1934. J. A. M. A., Volume 103, No. 19, Page 1425; November 10, 1934.

Although this article has no immediate gastroenterological application the results are so extraordinary that probably every system in the body will be affected when we understand more about the mechanism of the results obtained by the injections of Thymus Gland Extract. The authors point out that the most striking biologic effects of thymus extract (Hanson) are obtained and are most evident in the offspring following continuous treatment by intraperitoneal injection of successive generations of rats.

The authors conclude that thymus extract (Hanson) has accelerated the rate of growth and development, has hastened the onset of adolescence in the offspring of treated rats, and has seemed to increase the fertility of parent rats, and that the injection of succeeding generations of parent rats has resulted in the amplification of the effects of thymus extract.

Samuel Morrison, Baltimore, Maryland.

SECTION IX- *Book Reviews*

This Journal is not responsible for the opinions, decisions or grouping expressed by reviewers of books or pamphlets. For the guidance of readers, an attempt is made to indicate the relative worth of reviewed material by placing "stars"—★ in connection with the reviews. The greater the number of "stars," the more agreeably and importantly has the book or pamphlet impressed the reviewer.

Amebiasis and Amebic Dysentery

By

CHARLES F. CRAIG
SPRINGFIELD, ILL., and BALTIMORE, MD.
C. C. Thomas, 1934, viii+315 pp.

IT IS particularly timely that a book on amebiasis and amebic dysentery should be written, following as it does upon the now classical outbreak of amebiasis in Chicago in 1933. This outbreak acted as a stimulus for finishing up a work which the author had been anticipating as the result of his thirty years of study on the subject.

The book is written for the medical profession with the hope that it will prove helpful in the diagnosis, prophylaxis, and treatment of amebiasis. While "amebiasis" is a term which includes amebic dysentery, one of the outstanding symptom-complexes of the disease, for the sake of clarity the author has added "amebic dysentery" to the title because so few physicians apparently realize the true meaning of the word "amebiasis".

In the introductory chapter, the author discusses the historical aspects of the disease from Lösch's discovery of the parasite in 1875 to the present date. He deals with the geographic distribution, pointing out that the disease is world-wide. In the United States, he estimates that the incidence is from 5 to 10 per cent, and that at least 50 per cent of the affected individuals have definite symptoms caused by the presence of the ameba. Under the heading, "Etiology of Amebiasis and Amebic Dysentery", one finds a brief discussion of the classification and nomenclature of the parasite; the acceptance of the *genus*, Endamoeba, Leidy, 1879, to contain *histolytica, coli,* and *gingivalis;* the *genus* Endolimax Kuenen and Swellengrebel, 1917, to contain *nana;* Iodamoeba Dobell, 1919, to contain *bütschlii,* and Dientamoeba Jepps and Dobell, 1918, to contain *fragilis.* Then follows a detailed account of the morphology of *Endamoeba histolytica* with particular emphasis on the type of motility of the trophozoite. This the author describes as being typically slug-like and suggests that the ameba has a definite polarity. This is of considerable importance since the general impression is that the typical motion of *Endamoeba histolytica* is by means of explosive pseudopods. The author refers to the encysted stage as the "cystic stage" which, although technically probably correct, is not commonly employed. Col. Craig has lapsed into a common error in referring to the cysts as being round or oval when, in reality, the cysts are either spherical or ovoid, a distinction of considerable importance in a proper understanding of the morphology of these forms. He has seen no chromosomes in spite of the fact that Kofoid and his co-workers have described in detail the chromosomes, the mitotic division, and have stated that the number of chromosomes in *Endamoeba histolytica* is six. The author in this respect agrees with the English workers and with most others that the method of reproduction is a modified mitosis and that chromosomes cannot be distinguished. He discusses briefly the experimental infection of lower animals with *Endamoeba histolytica* and points out that there is no question but that the organism is pathogenic for man.

The third chapter deals with epidemiology and one finds a table of surveys in foreign countries indicating the percentage of infection to range between 1.5 and 50.87 per cent. A table for the United States embracing 49,336 cases gives an average instance of 11.6 per cent. Craig, through an error, states that Sanford reported 1,135 cases of amebiasis in 5,000 patients or a percentage infection of 22.5 per cent. As a matter of fact, Sanford reported 500 cases, 12.0 per cent. Craig's error is due to an error in table headings in Sanford's paper. One should, however, call attention to the fact that these surveys are not typical of the civilian population but frequently represent sick people and persons confined in institutions of various kinds. It is, therefore, some

question as to whether one may draw conclusions too definitely from such surveys as to the instance of amebiasis. The author, however, takes a conservative view of the matter and points out that even if the instance were only one-tenth of this figure, there would be more than a million cases in the United States alone. He still believes that the most common method of transmission of the disease is by food handlers who are carriers of the infection although he enumerates many other possible and probable methods of transmission, pointing out that in the Chicago epidemic, the method was undoubtedly by contaminated water.

Craig recounts the many experiments dealing with the viability of the cysts. The conclusion of the presentation is that the cyst is capable of withstanding the vicissitudes of nature for a long time. When one recalls that there must be countless numbers of cysts discharged by means of the sewage into the same water that is subsequently used for drinking purposes in many localities and that these cysts are viable for a long period of time and that this water is consumed in large quantities, it will be necessary to offer more positive evidence than has yet been offered to substantiate the statement that the most common means of transmission of amebiasis is by food handlers, even if many such are carriers. Craig believes that while there might be some difference in virulence of strains, the most important factor in the development of the disease is the degree of resistance of the host. All of the epidemics which the author cites, of which there are not many, have been among soldiers with the single exception of the outbreak in Chicago.

The next two chapters deal with the pathology of the disease. The author believes that all carriers have lesions of some type and that cytolysis and necrosis of superficial epithelium of the intestinal tract is constantly taking place. He recounts in some detail the experiments which have been performed upon animals and comes to the conclusion that the lesions in the dog are nearer like those in the human than are those produced in the kitten; he suggests that certain conclusions which have been drawn from experimental work on kittens are not applicable to the human. After a detailed discussion of the pathology in acute amebic dysentery, the author deals with the pathology of abscesses in the liver, lung, brain, and of the infection of the skin. Craig is not willing to accept Kofoid's conclusion that these organisms invade the joints in arthritis and the lymph nodes in Hodgkin's disease, pointing out that no one has confirmed these findings.

Under the chapter heading, "Symptomatology", there is a complete discussion of the symptoms of the healthy carrier, the carrier who is considered healthy but has very mild symptoms, the patient having recurrent attacks of amebiasis, and acute and chronic amebiasis and amebic dysentery. Under "Complications", the author lists as definite but relatively rare complications, abscesses of the liver, lungs, brain, spleen, infection of the skin, amebic appendicitis, peritonitis, intestinal perforation, acute hemorrhage, possible infection of the urinary tract, and some other extremely rare complications. The sequelae are usually confined to adhesions and contractions and the results thereof.

Two chapters are devoted to the diagnosis of amebiasis. After dealing with general methods of clinical diagnosis, he gives an extremely detailed account of the morphologic differences between *Endamoeba histolytica* and the other four intestinal amebas. He discusses the technic of diagnosis from smears, both unstained and stained. The details of cultural methods are enumerated and a section is devoted to the diagnosis of amebas in culture. This is not as convincing as one would desire and leaves one with some doubt that an unknown ameba growing in culture can be precisely identified. As the most recent method of diagnosis of amebiasis, the author gives an account of the complement fixation test which he has devised and which has been modified by Tsuchiya and by Weiss and Arnold. He is modest in his claims for the usefulness of the test, clearly stating that he believes the most important method of diagnosis is examination of the stool. He cautions that modifications of the test should be tried in hundreds of cases of amebiasis as well as in normal individuals and as he has done in the past, points out that the chief limitation of the test at the present time is the difficulty in preparing a suitable antigen.

In a discussion of the prognosis and prophylaxis of amebiasis, Col. Craig calls attention to the fact that the prognosis is good in acute cases but should be guarded in chronic and recurrent cases and that abscesses complicating amebiasis make the life of the patient hazardous. The prophylactic measures he advocates are, careful attention to personal hygiene, treatment of carriers, careful attention to the rules laid down by the committee investigating amebiasis in Chicago, and the proper disposal of the feces of carriers. He points out the difficulty of enforcing laws concerning food handlers and rather cautions against too drastic measures.

The final chapter deals with the treatment of the disease with a description of the drugs used and the definite statement that there is no single drug and no single method of treating this condition. He believes that the safest and best treatment for the carrier is with "chiniofon", that during the stages of acute dysentery, emetine should be used with caution and understanding, followed by chiniofon or perhaps some other of the modern drugs. He discusses the advantages and disadvantages of the puncture and aspiration method of treatment of abscesses as against the open operation. In either event, he advocates the use of emetine.

The book is liberally illustrated with fifty-four cuts which are excellent. They are, for the most

part, from the material in the Army Medical Museum collection, a great deal of which Colonel Craig personally collected. The composition and appearance of the book are pleasing, and the liberal use of bibliographical references will make an appeal to the more careful student of the subject. If one carefully reads the text, one is impressed with the thorough knowledge Colonel Craig has of the subject and with the fact that his long years of teaching have given him a method of presentation which is altogether desirable.

Certainly during the past thirty years Colonel Craig has developed into the outstanding authority on amebiasis in this country and his book will be welcomed and enjoyed as a fitting climax to his years of study.

Thomas B. Magath (Rochester, Minn.).

ABSTRACTS

TUCKER, C. C., AND HELLWIG, C. A.

Histopathology of Anal Crypts. Surgery, Gynecology and Obstetrics. Vol. LVIII, No. 2, February, 1934, pp. 145-149.

The authors studied histologically 331 hemorrhoids and 89 infected rectal crypts removed surgically. In uncomplicated cases of cryptitis they found the crypts of Morgagni to be normal, but without exception they found that the pathological process had its origin in narrow duct-like structures which opened into the crypts of Morgagni. Those duct-like structures were either simple tubules, or complex branching ducts, which extended from the mucosa of the crypt into, or through, the muscular coat of the bowel, and ended blindly in connective tissue.

In acute infection these ducts were filled with pus, and their walls infiltrated with leucocytes. The walls of these ducts were lined with epithelium showing that they were not fistulous tracts caused by a burrowing of an inflammatory process from the anal crypts. The mucosa lining these ducts was stratified, squamous near their openings, while farther out they were lined with transition epithelium, and finally columnar epithelium. By examining surgical and post-mortem specimens without inflammatory change the authors found in most cases well developed tubular structures extending from the crypts into the submucosa or sphincter muscles. No case showed true glandular structure in connection with these ducts.

To obtain more information about the biological significance of these structures the anal regions ot rabbits, cats, dogs and guinea pigs were examined. In all of those animals the authors found more or less well developed glands opening into the crypts of Morgagni at about the same location as those found in the human. The function of these glands is a matter of conjecture; they may secrete a lubricant or an odoriferous substance.

These small preformed ducts communicating with the bowel as they do, afford a ready path for such infective organisms as are found in the bowel to invade the surrounding tissues. The existence of these preformed epithelial lined tubules explains the clinical fact that cryptitis and anal fistulae do not heal by conservative treatment. Small areas of epithelium not destroyed by the infection of these ducts and not removed in the treatment of their infection persist to prevent obliteration of the ducts by scar tissue. It has been said that infection of the crypts of Morgagni (and also of these ducts) is probably the most frequently overlooked source of focal infection that is present in the human body.

The authors conclude that these ducts are remnants of a complex glandular structure as found in the lower orders of mammals.

Nelson M. Percy.

RANKIN, FRED W.

"Multiple Polyps of the Colon." South. Med. Jour., 27:574-578, July, 1934.

Polyps of the colon whether few or diffuse are important first, because of their tendency to undergo malignant degeneration, and second, their tendency to cause obstruction. All pathological types of benign tumor are found in the large bowel and, being pedunculated, may be termed polyps. There are in general two varieties of multiple adenomas or polyps of the large bowel; one, a true adenoma of congenital origin, and the other, a pseudo variety secondary to some chronic inflammatory condition such as ulcerative colitis. Corresponding to the incidence of cancer polyps are eight times as common in the sigmoid and rectum as in the rest of the colon. The degree of involvement of the gastrointestinal tract together with the amount of obstruction or ulceration caused by it determines the clinical course of the disease. The symptoms of multiple polyposis are diarrhea with the passage of blood or mucus in the stool, pain occasionally accompanied by nausea and vomiting, weakness and loss of weight. The diarrhea is especially significant if it is intermittent, recurrent, and progressively more severe. Rectal tenesmus is in direct proportion to the closeness of the lesion to the anal sphincter. Digital, proctoscopic and radiologic examinations confirm the diagnosis (in the latter the "combined double contrast" method of Fischer or one of its modifications is recommended).

Surgical treatment may consist of transperitoneal colostomy with excision of large polyps, the resection of a segment of colon, or total colectomy which may or may not include the rectum. The first two procedures are not especially formidable but the removal of the entire colon involves a grave risk. If the rectum can be saved the ileum can be transplanted into it. If not, the following three-stage procedure used without mortality by the author in six cases (only three of which fall into this group under discussion) is recommended: ileostomy, subtotal colectomy down to or near the recto-sigmoid junction, and then a combined abdominal-perineal resection of the recto-sigmoid and rectum.

J. Duffy Hancock.

MORGAN, JAMES W.

Pectinosis and Minor Maladies of the Anal Region. S. G. O., 59:806-809, November, 1934.

The four major landmarks of the anal canal are clearly defined: the anocutaneous line at the exterior of the anus, the white line of Hilton just external to the pectinate or dentate line which latter marks the location of the anal crypts, and the uppermost limit of the anal canal, the anorectal line. The writer describes the anorectal line as being found 1.5 centimeters above the dentate margin, recognizable through the microscope by a transition from cuboidal epithelium to the deep columnar epithelium of the rectum above the columns. The writer follows Miles and other English surgeon-proctologists in emphasizing the importance of fibrous deposits in the *pecten*, that area bounded by Hilton's line below and the dentate margin above, and advises linear section of consequent fibrous bands.

Curtice Rosser, Dallas, Texas.

An Instance of

Syphilis of the Stomach*

(In Congenital Lues)

By

V. C. ROWLAND, M.D.

and

E. E. WOLDMAN, M.D.

CLEVELAND, OHIO

THE following report of a gross deformity of the stomach in a congenital luetic with a prompt and striking response to specific therapy seems worthy of placing on record.

It deals with a 20-year-old, undersized son of known syphilitic parents, the patient having definite stigmata of congenital syphilis, including typical interstitial keratitis, prominent frontal bosses, high palatal arch, defective teeth and a positive Wassermann reaction.

CASE REPORT

L. D., white American boy with past history quite negative except for the active stage of his eye disease at six years of age and impairment of sight since that time. He came to the gastro-intestinal clinic July 17, 1929, complaining of epigastric soreness immediately after eating for a period of three weeks. He refused to take anything but liquids on account of the distress and rapidly lost weight from 140 to 109 pounds. He gave a history of similar but milder symptoms for a period of three weeks, a year before, but was almost free of all digestive symptoms after that time until the present disability.

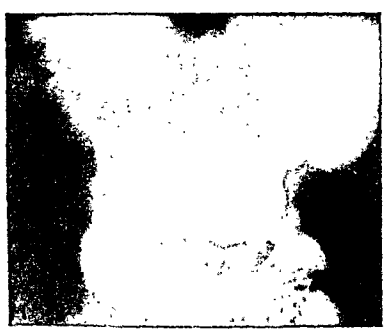
General examination was largely negative. The corneae showed the ground glass steaminess of an old keratitis. The pupils were somewhat sluggish in reaction, the right slightly larger. The teeth, which were described as "stubs", all were extracted in 1926. The chest and abdomen were entirely negative.

Gastric analysis showed complete absence of hydrochloric and total acid even after .3 mgms. of histamine. No lactic acid, blood, pus or Boas-Oppler bacilli could be demonstrated. An Ewald meal aspirated at the end of an hour yielded 200 c.c.

Blood chemistry showed sugar, 82; urea nitrogen, 10; uric acid, 2.5; N.P.N., 37; NaCl, 430; CO_2 combining power, 63.6; blood Wassermann, four plus; Kahn, four plus; spinal fluid Wassermann, negative; cells, 2—faint trace of globulin; icteric index, 20.7; hemoglobin, 12.6 gms.; liver function test (Bromsulphalein), five minutes, 30 per cent—fifteen minutes, 15 per cent; white blood count, 9750; urine entirely negative.

On July 18, 1929, *fluoroscopic examination* showed a small "sclerosed" stomach and in the mid and distal portion of the stomach a marked irregular defect interrupting peristalsis and strongly suggesting malignancy.

Fig. 1. Before treatment—Funnel shaped, semi-rigid contracture of the pyloric end of the stomach, resisting belladonna bromides and amyl nitrite at the time of fluoroscopy. No peristalsis over the affected area. Pylorus free.



(Fig. 1). He was given antispasmodics, belladonna, and luminal for one week.

On July 26, 1929, *X-ray* showed the deformity unchanged with an extraordinarily rapid emptying of the stomach, it being nearly complete in five minutes. Amyl nitrite was used at the time with no effect upon the deformity.

He was treated in the ward from July 27, 1929, to August 10, 1929. While under observation, it was obvious that he was afraid to eat on account of distress which he said was never severe pain. There was no vomiting. He lost weight to approximately 103 pounds. Alkalies aggravated the symptoms.

On July 31, 1929, .3 neosalvarsan was given and iodides by mouth; a few days later .45 neosalvarsan.

On August 4, 1929, he first stated that he felt better; on August 6, definitely better.

On August 8 the patient was eating with comfort.

On August 10 he claimed to be free from distress and left the hospital because he felt "cured". There was an interruption of treatment, unfortunately, for about two months during which period he gained 30 pounds in weight.

On October 26, October 29 and December 12, injections of .45 neosalvarsan each were given. He claimed to be entirely free of symptoms, weighed 133½ pounds and the X-ray deformity and concomitant signs largely had disappeared.

On April 19, 1931, the last film was taken. This showed practically a normal stomach except for indentations on the greater curvature.

COMMENT

Gastric syphilis is sufficiently rare (60 in 10,000 cases of syphilis—Stokes) as to escape

*From the Gastro-Intestinal Clinic of the St. Luke's Hospital, Cleveland, Ohio.
Received for publication September 10, 1931.

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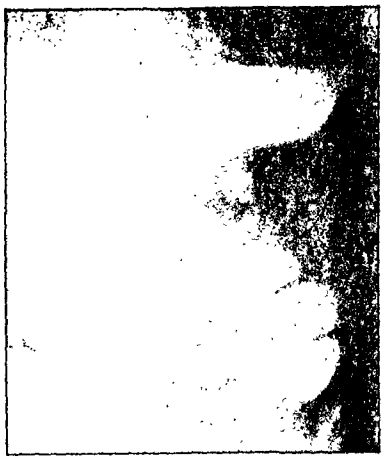


Fig. 2. Before treatment—Taken a day later than Fig. 1. Concentric, tubular deformity persists. Rapid emptying.

consideration until advanced changes force the suggestion of an unusual condition. Its incidence probably is less than 1 per cent of visceral lues (Crohn) and still less in the congenital form of the disease (Stokes). It is not commonly looked for or recognized in an early stage. In the late stage, fibrotic contractures complicate the diagnosis and may prove refractory to medical treatment. Since the diagnosis never can be made with absolute certainty except by tissue inoculation as was done by Harris and Morgan in 1932 *(J. A. M. A.*, 99:1405; October, 1932), it is necessary to establish as clearly as possible the clinical picture of the disease. Even with surgical specimens available for pathological and cultural study, the demonstration of the true spirochaete of lues leaves some doubt as to the specimen's identity; the failure to find spirochaetes, however, does not exclude diagnosis of the disease. The same applies to the very characteristic perivascular round cell infiltration.

The lesions frequently are multiple and may exist as nodules, ulcers or gummatous infiltration with distortion, especially of the distal half of the stomach. They occur in younger individuals than do tumors of malignant type with symptoms extending usually over a period of a year or two without marked cachexia, although there may be rapid weight loss and some anemia. The blood Wassermann usually is positive but the spinal fluid often negative. Minor central nervous system signs, however, probably more frequently than visceral, or any other lesions, are associated with gastric syphilis. Usually there is a gastric achlorhydria (80 per cent) but not commonly gastric retention (15 per cent). Hypoacidity, Stokes regards as a characteristic tendency in all patients with syphilis at any stage. The most characteristic diagnostic criteria are:

(1) X-ray deformities suggestive of cancer with or without a palpable mass.
(2) A comparatively young individual.
(3) The presence of other evidence of syphilis.
(4) Prompt response to antisyphilitic treatment with rapid gain in weight and disappearance of digestive disturbances.

The Carman-Eusterman criteria, as tabulated by Stokes, are as follows:

Fig. 3. 10/26/29—Three months after beginning of treatment. The defect is less marked and the capacity of the stomach considerably increased.





Fig. 4. 4/9/31—Nearly 2 years after the beginning of treatment. Stomach practically normal except for indentation on greater curvature.

The Carman-Eusterman Criteria in the Diagnosis of Gastric Syphilis

CLINICAL	ROENTGENOLOGIC
1. Average age thirty-five years in contrast to average ulcer age of forty-five and cancer age of fifty-four.	1. Filling defect of gastric outline, usually without corresponding palpable mass.
2. Average duration of symptoms two years.	2. Hour-glass stomach (dumb-bell) or the upper loculus may be tubular, owing to extensive irregular concentric contraction.
3. Progressive as distinguished from intermittent course, except at outset.	3. Six-hour retention less frequent than in other gastric lesions (about 20 per cent).
4. Preservation of appetite, or ravenous, as distinguished from anorexia in cancer.	4. Diminution of gastric capacity.
5. Patient undernourished, but not cachectic. Condition better than the duration of the lesion, if cancer, would lead one to expect.	5. Stiffening or lessened pliability of the gastric wall.
6. Pain, gnawing in character, relieved by vomiting.	6. Absence of peristalsis from the involved area.
7. Evidence of low capacity, sense of fullness or bursting, ability to eat only small amounts, relief by vomiting.	7. Pylorus free rather than obstructed.
8. Achylia, achlorhydria, subacidity.	8. Patient usually under cancer age and not ill in proportion to the extent of the disease shown by the X-ray.
9. Retention infrequent.	9. Absence of a niche, accessory pocket or typical incisura; classical signs of simple gastric ulcer.
10. Hemorrhage unusual.	
11. Evidence of syphilis, clinical and serologic.	

An Unusual Instance of
Primary Myosarcoma of the Stomach with Recovery Following Operation*

By

M. E. GABOR, M.D., M. TUFTS, M.D.,

and

W. C. F. WITTE, M.D.

MILWAUKEE, WISCONSIN

SARCOMATA of the stomach are exceedingly rare. The majority of textbooks merely mentions the existence of such tumors. Statistics of the Mayo Clinic and those from other sources place the incidence of gastric sarcoma between one and two per cent of all the tumors of the stomach. Appearing as extra-gastric neoplasms, they do not offer an entity complete enough to formulate a definite diagnostic syndrome clinically or roentgenologically.

Pathology: The pathological manifestations vary greatly and it is difficult to make a clear-cut histological classification. *Grossly,* the "exogastric" forms appear usually as sharply defined tumors and have either a peduncle or are "sitting" upon the stomach. The "endogastric" variety also may be pedunculated and often may be found moving around within the stomach proper. These tumors frequently invade the greater curvature, near to the antrum, and when they are pedunculated, extend beyond the limits of the stomach. In such event, they may attain enormous size. The origin of these tumors is in the submucous, muscular or subserous layers of the stomach. Often they undergo degenerative changes such as hemorrhage, necrosis followed by cystic formation, a condition which often causes difficulty in determining malignancy.

Microscopically, the tumors present a variety of round, spindle or mixed cells. An admixture of other cells (fibro or myosarcomata) with subsequent secondary degeneration often renders a thorough histological diagnosis problematical. The round-celled sarcoma grows infiltratively, while the spindle-celled form tends to be localized; most of the exogastric tumors are represented by this class of cells. The former tumors exhibit a greater malignancy. Metastases relatively are rare, especially so in the case of the spindle-celled growths. A salient feature of such sarcomatous tumors appears to be a decreased malignancy. This fortunate circumstance allows such tumors to be treated surgically with success.

Symptomatology: The symptoms encountered are similar to those of retroperitoneal tumors. They may be classified as causing disturbances through pressure into two groups.

In the *first group,* the tumor is small and accompanied by obscure digestive symptoms which cause the patient little appre-



*From the Medical and Surgical Services of St. Mary's Hospital.
Submitted November 12, 1934.

hension. In the *second group,* the tumor is large, the patient has gastric distress, vomiting, the appetite is poor, the function of the gastro-intestinal tract is irregular, alternating with constipation and diarrhea. Definite pain often is substituted by distress. Often there is a pronounced anemia and there may be cachexia. Hemorrhage is fairly frequent, mostly in the form of melena.

Differential Diagnosis: The position of the tumor in the upper abdomen either to the right or the left side easily is confused with other tumor masses developing in this region; special study may be needed to eliminate the knowledge of the presence of tumors other than the sarcomata being discussed. Especially must the following differential possibilities be considered: *(a) Carcinoma of the stomach:* Here a thorough X-ray study may eliminate doubtful cases. In carcinoma, a careful visualization of the irregularities of the mucosal folds may reveal defects characteristic for malignancy; in sarcomatous growths, the mucosa commonly is intact—a significant point in the evaluation of these tumors. *(b)* Other extragastric tumors such as *submucous myomata*—large pedunculated polyps occurring especially in the cardiac end of the stomach. *(c) Banti's disease* with gastric hemorrhage. Gross tumors in the splenic region associated with secondary anemia may be very confusing and a differentiation almost impossible. *(d) Pancreatic cysts. (e) Retroperitoneal tumors,* such as sarcomata of the mesentery and mesenteric cysts, — mixed tumors of kidneys and suprarenal cysts of spleen. *(f) Tumors of the bladder or ovary.* Here a cystoscopic examination or special gynecological examination may clarify certain doubtful lesions.

Treatment: Surgery alone is able to accomplish possible results. According to numerous observers, a complete cure has been achieved by complete removal of sarcomatous or fibrosarcomatous tumors of the stomach. They are, as a rule, easy to resect without the surgeons being compelled to remove a large portion of the stomach, a fact which is very important in debilitated patients.

Prognosis: Good in view of the relatively scant metastases.

CASE REPORT

Mr. A. M., age 54, American, married, city-credit agent, came in on account of "indigestion", and a "tightness" at the belt line. His appetite was poor, he had pains after partaking of food, cramps occasionally and dull aches and distension almost constantly. He vomited frequently; the vomitus consisting of food and bile but never blood; he had noticed tarry stools and had suffered from intermittent diarrhea. He experienced dyspnea occasionally and had difficulty in working because of exhaustion. The patient had lost twenty pounds in weight during the previous six months.

Physical examination: Emaciated male, with poor panniculus. Slightly

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(Ca=.21, P=.36, Fe=.005)		
Cellulose substances, Pentosans, etc. (by difference)	6.	—
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subicteric skin; visible mucous membranes pale, tongue coated, teeth in poor condition; reflexes were normal; no thyroid enlargement or general adenopathy. Heart was normal in size and the sounds were clear; lungs were grossly normal except with few crepitations in the left base, posteriorly.

Abdomen: There was a huge mass in the upper, midportion of the abdom; it was the size of a man's head and extended more to the left than to the right. It was of firm consistency; following respiratory movement it could be fixed in the epigastrium. It was slightly movable, protruded prominently and was fairly sharply circumscribed.

The laboratory examination revealed a slight hypochromia; Hgb. 54 per cent, R.B.C. 3,980,000, W.B.C. 11,300. Urine: slight trace albumin with occasional casts.

The *X-ray examination of the stomach showed:* The viscus was displaced upwards and displaced markedly to the right. The outlines of both curvatures were sharply defined. However, the lower portion of the greater curvature near the antrum presented a pouching the significance of which could not be determined precisely at the time of the examination. The duodenum was normal. Emptying of the stomach was considerably delayed. Twenty-four hours after the barium meal, the colon was filled throughout. The roentgen picture was typical for an extrinsic tumor exercising a downward pressure upon the ascending and descending portions of the colon. On refilling the stomach at this time no connection between this organ and the colon was found.

A tentative diagnosis of an abdominal tumor of retroperitoneal origin was made. A malignancy was considered (possibly a sarcoma of the mesentery or a pancreatic cyst) in view of loss of weight and cachexia.

Surgical exploration was advised and performed on August 26, 1933, by Dr. W. C. F. Witte at St. Mary's Hospital. By a left rectus incision, the lesser peritoneal sac was opened; a mass the size of a large grapefruit was found. It was situated in the posterior chamber and attached to the posterior wall of the stomach by a narrow base. It appeared to be a large multilocular cyst, filled with clotted blood and was adherent to the surrounding tissues. It was attached to the stomach by a small, thick stem which could be followed into the inner structures of the muscularis. A portion of the posterior wall of the stomach was resected in order to remove the tumor intact.

The post-operative course was uneventful and the patient left the hospital in three weeks. A course of X-ray therapy followed the surgical procedures.

Pathological report: The histological examination revealed spindle-celled myosarcoma with cystic degeneration and hemorrhage.

Progress: The patient resumed his work, returned to normal weight and has had no evidence of recurrence to the present date.

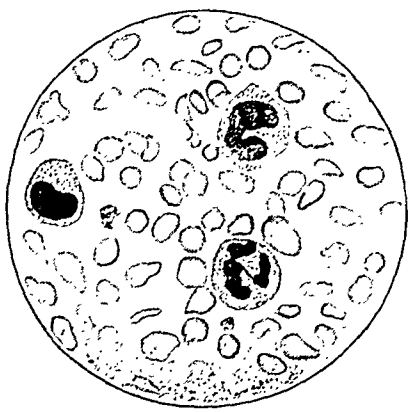
SUMMARY

A case of myosarcoma of the stomach is reported.

Surgery is indicated in this type of neoplasm since operative removal usually is followed by good results because metastases are uncommon. Radical resection of the stomach often can be avoided inasmuch as tumors of this type exhibit sharp demarcation from the remainder of that viscus.

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ABSTRACTS

HERRMAN, WILLIAM G.

A case of right sided atypical diaphragmatic hernia. Radiology 22:241-246, 1934.

Diaphragmatic hernias are commonly classified as congenital or acquired, traumatic or non-traumatic and "true hernias" (with an hernial sac) or "false hernias" (non-saculated). The commonest sites for congenital herniation, which presuppose embryologic weakening, are: 1. The esophageal opening. 2. The *hiatus pleuro-peritonealis* (foramen of Bachdoleck). 3. The dome of the diaphragm. 4. The *foramen Morgagni*. 5. A congenital absence of the left half of the diaphragm.

Non-traumatic hernias which develop after birth usually have an enclosing sac. Traumatic herniation commonly occurs through the esophageal opening, in which case there is apt to be a sac, or through the posterior portion of the left diaphragm, when there is usually no sac. Herniation through the diaphragm on the left side is not so uncommon as was thought in preroentgen days.

The author reports a case to which he has been unable to find a parallel in the literature of recent years: *The patient*, following a roentgen study, was explored surgically and later at necropsy and more detailed information obtained. A 17-year-old, slender, colored female emaciated from pernicious vomiting of four days' duration, gave no history of previous gastrointestinal disturbance. The abdomen was scaphoid. The right chest gave signs of hydropneumothorax. *X-ray study* revealed right sided herniation of the pyloric end of the stomach and duodenum through the right posterior diaphragm, with obstruction below this point. Operation and autopsy demonstrated this to be through the mesial lumbo-costal arch behind the outer *crus*, involving the distal half of the stomach and six inches of duodenum. There was a well-defined ring in the diaphragm, and the herniated viscera were covered with a sac which occupied the inner lower portion of the right pleural cavity and measuring about six inches in diameter. The stomach was adherent to the sac at its apex. Appreciable inflammatory change, *petechiae* in the mucosa and serosa of the stomach and duodenum were present from the strangulation. Death was due to high, strangulate, intestinal obstruction which depressed the patient's reserves beyond her power to react to antishock measures postoperatively.

James T. Case, Chicago, Ill.

TAMIYA, CH., AND NOSAK, SCH.

Diagnosis and Therapy of Pedunculated Tumors of the Oesophagus. Fortsch, auf dem Gebiete d. Roentgen Strahlen, May 1, 1934, B 49, H 5.

A pedunculated fibroma of the oesophagus is reported. The roentgenological visualization was established by a special method and the tumor was removed at oesophagoscopy. The patient enjoys good health one year after the complete removal.

This is the thirteenth case of non-malignant tumor of the oesophagus reported in the literature.

Roentgenological examination is of paramount importance and the employment of seriological pictures in upright position is stressed. The patient is rotated to about 90 degrees and aimed exposures are made at different angles giving almost plastic impressions. This technique is equal in value to that of Palugyai's (air insufflation).

In contrast with carcinoma of the oesophagus there is no "axis-stenosis" to be found but rather a central shadow with a perifocal stenosis. The latter has a tendency of having striated contours. The walls surrounding the tumor are not rigid and the peristaltic activity is not lost. The peduncule is displayed by a characteristic defect of the shadow. Differential diagnosis does not offer difficulties as other pathology (carcinoma, struma, aneurysm, varices, mediastinal tumors) easily is ruled out. The case presented by the authors is illustrative in that not every suspicious tumor of the oesophagus is carcinoma but if such non-malignant lesions are diagnosed in time, patients' lives can be saved.

M. E. Gabor, Milwaukee, Wis.

ALLEN O. WHIPPLE, M.D., F.A.C.S., AND THEODORE S. RAIFORD, M.D.

The Type and Grade of Gastric Carcinoma in Relation to Operability and Prognosis. S., G. and O., 59:397-409, September, 1934.

The most interesting and practical part of this comprehensive paper is that concerned with the pre-operative determination of the type of tumor and the grade of malignancy. The records show that those patients giving a rapid fulminating history of carcinoma are most apt to harbor a growth of relatively greater malignancy. The same is true of those giving a history of an ulcer of several months progressing steadily and failing to improve after conservative treatment. On the other hand those giving clinical manifestations of no great severity, which develop slowly over a period of several months, are in the majority of instances Grades I and II. Gastric analyses show the percentage of achlorhydrias is greatest in the fungating type, least in the carcinoma-on-ulcer type, greatest with tumors located in the pars media, least in the pylorus. On physical examination the large fungating tumors are the type most likely to be felt.

In addition to these criteria the authors discuss the X-ray evidence, pathological studies, and operative findings in the various types. They believe that more accurate results could be obtained if the cases were studied by a gastroduodenal clinic consisting of a surgeon, physician, roentgenologist, and pathologist. They rather accept the rules of Lahey and Jordon for limiting the conservative treatment to those who within a period of three weeks are symptom free, whose lesion, by X-ray study, shows a definite decrease in size, and whose feces and gastric contents show a disappearance of blood entirely. The article ends by quotations from Maes and Curtis, indicating that exploratory laparotomy has a definite place even in those cases where accurate diagnosis cannot be made otherwise—remembering that "in malignant disease the certainty of diagnosis is frequently also the certainty of death" and that "it is better to have a less accurate diagnosis and a more favorable prognosis".

J. Duffy Hancock, Louisville, Kentucky.

G. MARAÑON, J. COLLAZO, L. GAETAN AND E. RODA.

Endocrinology. The Action of the Adrenal Cortical Hormone on the Elimination of Cholesterol by the Bile. 18:393-396, May-June, 1934.

The authors present evidence to suggest that in man and dogs the administration of suprarenal cortical hormone produces an increase in the cholesterol content of the blood and the bile.

Dwight L. Wilbur, Rochester, Minnesota.

GASTRIC MUCIN

A Physiologic Treatment for Peptic Ulcer

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IN the Alvarez Lecture* presented before the American Gastro-Enterological Society, May, 1933, Hurst stressed the fact that " It is a matter of common experience that mucus is rarely present in much excess, except in patients with hypochlorhydria or achlorhydria. This is due to the fact that the hypersthenic stomach is capable of secreting very little mucus compared with the hyposthenic stomach, whether in response to an irritant or as a result of inflammation (Bonis) Moreover, owing to the deficient power of secreting mucus, which is a characteristic of the hypersthenic stomach, the protection against damage afforded by a layer of mucus in the hyposthenic stomach is absent."

Gastric Mucin-Stearns is suggested to overcome this deficiency and thereby supply this protection.

In the questionnaire report compiled by Northwestern University Medical School on ulcer patients treated with Gastric Mucin, there were 226 intractable ulcer patients not responding to any other type of therapy. Of these, 137 were rendered symptom-free, 64 improved and there were 25 failures or recurrences while on Mucin Therapy.

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* A. F. Hurst, British Medical Journal, July 15, 1933, pages 89-94.

IN MANY digestive ailments, pathogenic bacteria resident in the lower bowel act either as direct causative agents or to aggravate lesions which have been initiated by systemic or constitutional deficiencies.

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CONTENTS

	Page
SECTION I—CLINICAL MEDICINE	
ANEMIA FOLLOWING OPERATIONS ON THE STOMACH—*Howard R. Hartman, M.D. and George B. Eusterman, M.D.*	829
THE RESULTS OF FAT TOLERANCE TESTS AND BLOOD SUGAR ESTIMATIONS PERFORMED ON PATIENTS AFFECTED WITH PEPTIC ULCER—*Maurice A. Schnitker, M.D. and E. S. Emery, Jr., M.D.*	834
AN INSTANCE OF GELATINOUS CARCINOMA OF THE DUODENUM—*J. Allen Wilson, M.D. and John F. Noble, M.D.*	840
SECTION II—EXPERIMENTAL PHYSIOLOGY	
THE APPLIED PHYSIOLOGY OF THE GASTRO-INTESTINAL INNERVATION—*A. C. Ivy, Ph.D., M.D.*	845
THE EFFECT OF MECHANICAL STIMULATION OF THE DUODENUM, COLON AND THE STOMACH ON THE CEREBRAL CIRCULATION AND INTRACRANIAL PRESSURE—*John Vandolah, M.S. and Lathan A. Crandall, Jr., M.D., Ph.D.*	853
SECTION III—NUTRITION	
GROWTH OF DIABETIC CHILDREN—*Henry J. John, M.D.*	855
THE NUTRITIONAL AND DIGESTIVE SYSTEM ASPECTS OF PERNICIOUS ANEMIA—*L. G. Zerfas, B.S., M.D., F.A.C.P. and Beaumont S. Cornell, M.D., F.A.C.P.*	857
ABSTRACTS	864
SECTION IV—THERAPEUTICS	
MEDICAL ASPECTS OF PEPTIC ULCER WITH SPECIAL REFERENCE TO DIAGNOSIS AND TREATMENT—*Arthur F. Chace, M.D.*	866
ABSTRACTS	870
SECTION VI—ABDOMINAL SURGERY	
DISEASES OF THE PANCREAS, ESPECIALLY ACUTE PANCREATITIS AND ITS TREATMENT—*John Douglas, M.D.*	87[illegible]
ABSTRACTS	879
SECTION VII—SURGERY OF THE LOWER COLON AND THE RECTUM	
MALIGNANCIES OF THE COLON WITH ESPECIAL REFERENCE TO THOSE OF THE RECTAL ZONE—*John F. Erdmann, M.D., F.A.C.S.*	881
ABSTRACTS	888
SECTION VIII—EDITORIAL	
THE "GRADUATE FORTNIGHT" ON DISEASES OF THE GASTRO-INTESTINAL TRACT RECENTLY CONDUCTED BY THE NEW YORK ACADEMY OF MEDICINE—*Frank Smithies, M.D.*	8[illegible]9
EXPERIENCE WITH BLOOD TRANSFUSION WHICH ADDS PROOF TO THE VIEW THAT AFTER A MEAL THE BLOOD CONTAINS UNCHANGED PROTEIN—*Walter C. Alvarez, M.D.*	891
THE JOURNAL ENJOYS ITS FIRST BIRTHDAY—*Beaumont S. Cornell, M.D.*	891
SECTION IX—BOOK REVIEWS	
BEITRAG ZUR KENNTNIS DES ILEUM TERMINALE FIXATUM UND ILEUS ILEI TERMINALIS FIXATI—*Peterson, Lennart*	892
SECTION X—AFTER "HOURS"	
HISTORY OF GASTRO-ENTEROLOGY—*Col. Fielding H. Garrison, M.D.*	893
SECTION XII—"THE CLINIC"	
HIGH RECTAL PAIN RELIEVED BY ELIMINATION AND ALSO BY "TEST-FREE" DIETS—*F. W. Bramigk, Ph.D., M.D.*	899
DYSTROPHIA ADIPOSOGENITALIS AND ITS RELATED DISTURBANCES—*C. Victor Richards, A.B., M.D.*	900
(INDEX NUMBER)	

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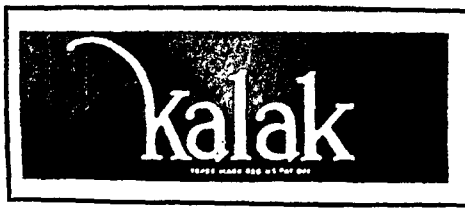
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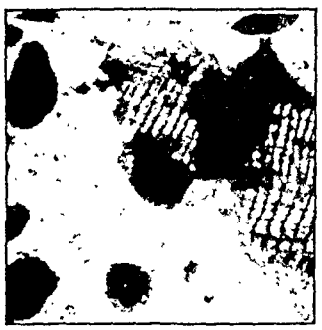
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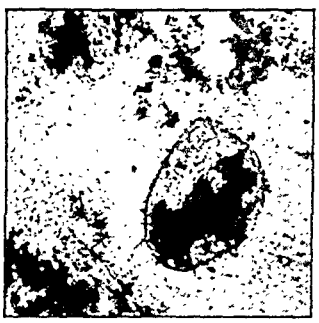
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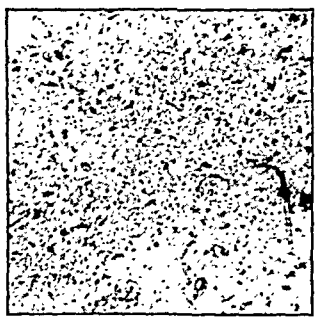
(Photomicrographs of stools diluted 7 times with water and stained with Lugol's solution.)



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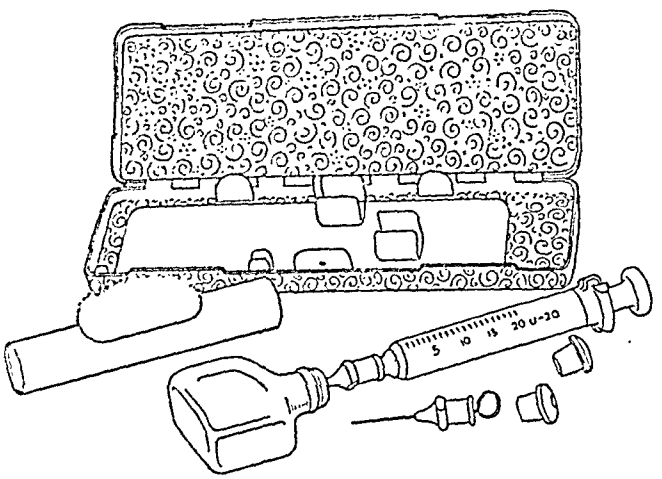
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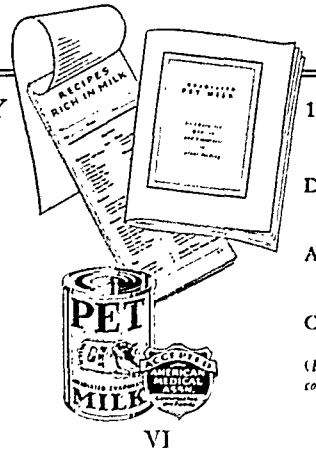
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SECTION I—*Clinical Medicine: Diseases of Digestion*

Anemia Following Operations on the Stomach *

By

HOWARD R. HARTMAN, M.D.

and

GEORGE B. EUSTERMAN, M.D.

ROCHESTER, MINNESOTA

GRADUALLY there has accumulated an appreciable number of cases in which total gastrectomy has been performed and many cases in which subtotal gastrectomy has been performed for diverse conditions. Coupled with cognizance of the fact that anemia of variable severity sometimes may follow operations on the stomach, a considerable literature on the subject has appeared in recent years.

For many years members of the medical profession have been impressed by the close relationship between achlorhydria and primary and secondary forms of anemia. The researches of Castle and his co-workers have demonstrated conclusively the presence in normal gastric juice of an activating substance that is necessary for hematopoiesis, and its absence in the gastric secretion of patients who have pernicious anemia. Therefore, theoretically at least, it is not illogical to conclude that total gastrectomy, removing as it does this intrinsic factor, should sooner or later give rise to pernicious anemia.

By the same token, subtotal gastrectomy, following which often only a small portion of the cardia remains, the mucous membrane of which may be the seat of chronic inflammatory changes, should produce the same result. Careful observers, moreover, have prophesied that all patients who have undergone gastrectomy eventually will have a primary or a secondary form of anemia. Notwithstanding this, cases of primary forms of anemia are comparatively rare. What may be the effect on the blood, over longer periods of postoperative life than usually obtain, remains to be determined.

Apart from the possible effects of the operation on the blood-forming function, occasionally we have observed the interesting clinical fact that pernicious anemia and gastric carcinoma may coexist in the same individual, and yet neither may bear an obvious causal relationship to each other. Also, occasionally, we have observed the hemogram characteristic of pernicious anemia in cases of benign gastric tumor; this type of tumor usually is associated with achlorhydria. Not infrequently the character of the blood count and the color index in cases of gastric carcinoma, especially in those cases in which the growths are of the advanced, diffuse form, are indistinguishable from those of pernicious anemia, although definite differences may exist from a morphologic standpoint.

PERNICIOUS ANEMIA

Pernicious anemia has been reported to have followed gastric resection for carcinoma, ulcer, and gastric syphilis, and even to have followed gastro-enterostomy for benign ulcer. This phase of the subject is well covered by the articles of Rowlands and Simpson, and of Goldhamer.

The first case of this nature observed in this Clinic was reported in 1921.

Case 1.—A white man, aged fifty-eight, was operated upon by W. J. Mayo, who performed total gastrectomy, including 1.5 cm. of the esophagus, for carcinoma of the posterior wall extending to within 4 cm. of the esophagus. The condition of the blood before operation was satisfactory: hemoglobin 80 per cent, and erythrocytes 5,520,000 per cubic millimeter of blood. There was no free hydrochloric acid in the gastric content. A little more than a year and a half following the total gastrectomy, the concentration of hemoglobin had been reduced to 55 per cent, erythrocytes ranged from 2,000,000 to 2,800,000 per cubic millimeter of blood and the color index was 1.2+; however, nucleated red blood cells were absent and there was no evidence of changes in the spinal cord. Roentgenologic and general physical examination revealed no evidence of local recurrence of the growth or of metastasis.

When the patient returned to this Clinic, thirteen months later, a history was obtained of frequent recrudescence and remission of anemia, and of severe attacks of epigastric pain in association with "bilious" vomiting and progressive decline. This patient also had chronic diarrhea. The stools contained excessive amounts of fat and undigested muscle fibers which might have been the result of chronic pancreatitis or jejunal disease or dysfunction. The patient lived nearly four years after the operation.

Case 2.—The second case to come to our attention, in which it seemed highly probable that pernicious anemia was present following gastric resection, was that of a white woman, aged forty-seven, who first entered this Clinic, September 4, 1920, because of "stomach trouble" and weakness. The patient's mother had died from carcinoma of the breast. The patient herself had had a number of infectious diseases, in addition to periodic sore tongue or aphthous stomatitis. Both oviducts and both

*From the Division of Medicine, The Mayo Clinic.
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ovaries had been removed nineteen years before because of chronic inflammatory pelvic disease. Appendectomy had been performed at the same time. The patient had had intermittent attacks of diarrhea since childhood, but in the ten years before we first saw her these attacks had been much more frequent and of longer duration and had been associated with moderate loss of weight. The stools had been profuse and liquid, and usually the first bowel movement of the day had occurred in the early morning. The woman had gone to stool two to six times daily in the course of an attack. Ten years before her admission, she first had experienced gastric disturbances. These had been characterized by "spells" of burning epigastric pain, which first had appeared two to three hours after meals and had been associated with nausea and regurgitation of salty, watery material. Food, but not alkali, had afforded relief. The last exacerbation, which had begun three months previously, had been associated with much weakness. On several recent occasions, the vomitus had contained 1 or 2 fluid ounces (30 or 60 c.c.) of bright red blood.

Examination disclosed that the woman was severely anemic, although she was fairly well nourished. She had a large mass in the upper part of the abdomen, extending to the left midclavicular line. Fractional analysis of the gastric content gave the following results: total acidity 10 units, no free hydrochloric acid in any fraction (both of the foregoing determined by Töpfer's method), no gross or occult blood, and a volume of 130 c.c. Roentgenoscopic and roentgenographic examination revealed an extensive filling defect in the stomach, beginning above the pylorus, extending well above the *incisura angularis*, and involving chiefly the posterior wall. The concentration of the hemoglobin was 40 per cent; erythrocytes numbered 3,200,000 and leukocytes 5,800 per cubic millimeter of blood and the color index was 0.6+. The percentages of the different types of leukocytes were as follows: polymorphonuclear neutrophils, 63.5; small lymphocytes, 27.5; large lymphocytes, 5.0; eosinophils, 3.0; and basophils, 1.0. There was slight anisocytosis, poikilocytosis, and polychromatophilia. Aphthous stomatitis, and a superficial ulcer on the tongue also were noted. The diagnosis was: extensive gastric carcinoma with marked secondary anemia.

Laparotomy, performed September 30, 1920, by W. J. Mayo, revealed an ulcerated, necrotic carcinoma of the posterior wall of the stomach, the lower border extending well beyond the *incisura angularis*. About two-thirds of the stomach, including the growth, was resected, and antecolic, end-to-side anastomosis of the Polya-Balfour type was made.

The patient was readmitted November 24, 1926, because of extreme weakness, edema of the ankles, dyspnea, puffiness of the eyelids, pallor, occipital headaches, occasional vertigo, non-productive cough, and transient numbness and tingling sensations in the hands. She had been aware of the paresthesia for the past three or four years, and of the anemia and its associated symptoms for at least six months. The diarrhea had ceased four months previously. For eighteen months following operation, at monthly intervals, the patient had been given a course of roentgen therapy in the hope of avoiding neoplasm recurrence. Transient arthritis of the right knee, tonsillitis, a "dry" cough, and cystitis had preceded the onset of the anemia. So-called "canker sores" on tongue and buccal mucous membrane also had persisted. Milk and eggs, and foods containing them, such as custards, provoked nausea, burning epigastric distress, and vomiting. The patient felt that the taking of hydrochloric acid had been very helpful.

Examination revealed no evidence of local neoplasm recurrence in the stomach or of metastasis to the liver, bones, peritoneum, lymph nodes, or *cul-de-sac*. Analysis now disclosed anemia of the pernicious type. The concentration of hemoglobin was 29 per cent and erythrocytes numbered 1,320,000 and leukocytes 2,600 to 3,200 per cubic millimeter of blood. The color index was 1.0+ and the volume index, 0.94. An occasional normoblast was found. Free hydrochloric acid was absent from the gastric content. On a diet high in liver and 1½ drams (6 c.c) of dilute hydrochloric acid, in water or in orangeade, with the meals, the concentration of hemoglobin increased to 70 per cent and the erythrocyte count to 3,140,000 in thirty days. The woman's general condition was much improved and she was dismissed from our observation December 28, 1926, with instructions to continue treatment under the guidance of her physician at her home.

Six years later, the patient's physician reported that the erythrocyte count was 4,648,000 and the leukocyte count, 6,200. Her blood pressure was 140 mm. of mercury systolic and 90 diastolic. She was still subject to attacks of vesical irritability, and to severe occipital headaches, which appeared early in the morning and which were relieved by taking "bromo-seltzer". Illness and deaths in the family, and serious financial losses, however, had caused considerable nervous fatigue and emotional stress. The patient was quite well in 1933 when she last was heard from.

Of great clinical interest is the fact that the above patient is alive thirteen years after gastric resection for extensive carcinoma. The diarrhea of long standing, and the condition of the mouth and tongue, which antedated the operation by some years, gave the impression that the patient may have had hereditary achylia gastrica and that eventually pernicious anemia would have developed whether or not she had had a gastric carcinoma. Moreover, although the subjective gastric complaint was highly suggestive of an ulcer before the development of carcinoma, the symptoms may have been the result of erosive or ulcerative gastritis which may have been a precursor to the carcinoma. Because we have no proof of the presence of achlorhydria in the earlier period of this woman's difficulty, the aphthous stomatitis and glossitis may have been of allergic origin, for such common allergenic substances as milk and eggs definitely disagreed with her, and the atrophy of the filiform papillae characteristic of pernicious anemia was not observed. Moreover, the anemia at the time of the operation definitely was of the secondary type, and the subjective manifestations of grave anemia, exclusive of paresthesia, were not present until about five and a half years after operation. One may speculate at length, but it is not unlikely that the anemia, which resembled that of the pernicious type, was a late, postoperative sequel, abetted by achlorhydria that was consequent on atrophic gastritis affecting the remnant of the stomach, or else abetted by focal infection, chronic diarrhea and inability to digest protein foods.

The fact that both patients whose cases have just been cited had diarrhea may be of considerable significance. In Case 1 there was evidence of apparent pancreatic insufficiency, at least of steatorrhea, of whatever origin, but in Case 2 examination for steatorrhea was not made. The diarrhea may have been the result of inflammatory changes in the small bowel, with resulting dysfunction of this organ of digestion and grave nutritional disorder such as is seen in idiopathic

steatorrhea. The blood picture in Case 2 may indicate hypochromic, megalocytic or erythroblastic anemia.

Of further interest are the instances of primary anemia developing following stenosis of the small bowel, or as the result of a gastro-jejunocolic fistula. An instance of the latter was reported by Fairley and Kilner. In their case the anemia disappeared after the fistula had been repaired. Furthermore, Rowlands and Simpson have expressed the opinion that the blood picture in cases of postoperative primary anemia is akin to that of anemia associated with idiopathic steatorrhea or to the various forms of tropical anemia, because the concentration of serum bilirubin usually is within normal limits, the Van den Bergh reaction is indirect and megaloblasts occur less frequently than in primary idiopathic anemia.

Case 3.—A white man, aged fifty-two, entered this Clinic April 5, 1915, with an abnormal gastric condition of two months' duration. This was characterized by a dull, constant, epigastric pain, which at the outset had tended to be projected toward the right iliac fossa, but later it had extended toward the left costal arch. Eating or drinking neither aggravated nor relieved the pain. Aside from stating that he belched and had lost 15 pounds (6.8 kg.) in the previous two months, the patient made no other complaint.

The *physical examination* gave inconsequential results, barring the fact that it revealed the presence of a poorly defined epigastric mass. The concentration of hemoglobin was 82 per cent; erythrocytes numbered 4,220,000, and leukocytes, 8,000 per cubic millimeter of blood. The total acidity of the gastric content was 6 units; and free hydrochloric acid was absent (both determined by Töpfer's method). Blood was present in the aspirated material. An opaque meal was not unduly retained. A roentgenogram of the stomach disclosed an extensive filling defect of the *pars pylorica*. The diagnosis was: carcinoma of the pyloric antrum without pyloric obstruction.

W. J. Mayo, who operated April 9, 1915, found an extensive carcinoma in the pyloric half of the stomach. The growth was large, fungating, necrotic, and edematous. Two-thirds of the stomach, including the neoplasm, was resected, and resection was followed by the making of a Mikulicz-Hartman-Polya type of anastomosis. The pathologic report was "carcinoma without involvement of lymph nodes". Convalescence was uneventful.

We are indebted to Dr. Harold Marsh, of the Jackson Clinic, for information concerning the patient's subsequent course. The patient was reëxamined May 2, 1922. He had been in good health until December, 1921, when, following an acute cold, he had begun to lose weight and strength, had become pale, and had begun to be dyspnoeic on exertion. In this interval of five months, he had lost about 15 pounds (6.8 kg.) and had become so weak that he had been able to climb stairs only with considerable difficulty. His mouth had been sore off and on. For six weeks before the examination he had complained of numbness of the fingers. He had not experienced any gastric disturbances since his operation.

The skin was of a lemon-yellow hue, and the mucous membranes were extremely pale. There was a localized systolic murmur at the apex of the heart. The spleen was not palpable. The concentration of hemoglobin was 40 per cent; erythrocytes numbered 1,950,000, and leukocytes 21,000 per cubic millimeter of blood. The percentages of the different types of leukocytes, based on a count of 200 cells, was as follows: lymphocytes, 38; polymorphonuclear neutrophils, 60; eosinophils, 1.5, and basophils, 0.5. Between May 9, 1922, and January, 1923, four transfusions of blood were given. In addition, the patient received elixir of iron, quinine and strychnine, Blaud's pills, and dilute hydrochloric acid. Subsequent examinations of blood gave the results recorded in Table 1.

Leukocytosis in pernicious anemia is unusual, but it has been reported to have occurred in the course of spontaneous remissions or following treatment with liver. Normablasts or megaloblasts were not found in Case 3.

The patient underwent a second operation, for enlarged spleen and anemia, elsewhere, October 27, 1923. Evidence of recurrent carcinoma or metastasis was not discovered. The patient succumbed to pneumonia a week later. Necropsy was not performed.

Morphologic studies of the blood have been found to be essential in the diagnosis of primary, hyperchromic anemia, for only rarely does sprue, with which it may most easily be confused, simulate it. Since such studies were not made routinely before 1928, we cannot unequivocally say that, in the cases cited, the anemia was of the pernicious variety. Future observations on patients who have undergone extensive or total gastric resection for gastric carcinoma, especially those who have achlorhydria, and who are fortunate enough to survive the operation for a number of years, coupled with modern hematologic methods of diagnosis, will determine whether anemia of pernicious type is an end result of a coincidence.

According to Watkins, who furnished us the following data, in pernicious anemia, the characteristics of the erythrocytes are as follows: 1. The cells are larger than normal (macrocytosis). 2. Poikilocytosis, or cells the shape of a pear, with a tendency of most of the cells to be elongated, is present. 3. The content of hemoglobin ordinarily is normal, resulting in normochromasia. 4. Usually some very small erythrocytes, about a half to a third the size of a normal cell will be found. These cells, when found along with the macrocytes, practically are diagnostic of pernicious anemia, for they do not occur in sprue.

The same authority lays down the following as distinctly characteristic of the leukocytes: 1. There is a shift of neutrophils to the right, which means that the number of lobes of the nuclei is increased. 2. There is a good deal of thinning and "stranding" of the individual lobes.

Other morphologic features found in pernicious anemia, again according to Watkins, are also present in other severe types of anemia and are not diagnostic.

Primary forms of anemia which may develop after gastro-enterostomy for peptic ulcer never have been observed in our cases. In view of the enormous number of cases in which gastro-enterostomy is performed, this lack of instances of anemia must be looked on as the result of coincidence only, because we have seen cases of pernicious anemia in which there have been antecedent symptoms and signs of gastric or duodenal ulcer. It is not unlikely, however, that the achlorhydria which follows the operation may have hastened the development of anemia in patients predisposed to its development.

The rarity of primary anemia following extensive gastric resection, in our experience and in

that of other physicians of representative clinics is supported by the results of experimental investigations. Judd and Marshall and Walters have followed several of their patients who had been subjected to total gastrectomy, and none had suffered from development of a primary form of anemia at the time of the follow-up studies. Mann and Graham observed six dogs, on which total gastrectomy had been performed, for periods varying from eighteen months to six years. In none of the animals did anemia develop which could be ascribed to the loss of gastric tissue. Ivy, Richter, Meyer, and Greengard reported absence of pernicious anemia among dogs that had been subjected to total gastrectomy, and some of the dogs had been observed for as long as ten years. The investigators named were of the opinion that pernicious anemia following gastrectomy was an accidental happening, in all probability. Goldhamer performed total gastrectomy on eight *macacus rhesus* monkeys, and reported that the specific blood picture of pernicious anemia of man did not develop within the six months' period of observation, although certain features of pernicious anemia could be discerned in the blood picture. The infrequency of pernicious or hyperchromic, macrocytic anemia following subtotal or total gastrectomy for carcinoma or benign gastric lesions, in our experience, inclines us to the same viewpoint as that adopted by the experimental physiologists.

However, the experimental animal may not be identically comparable biologically and pathologically with the human patient who harbors gastric carcinoma. Therefore, one should keep an open mind as to the possibilities of grave, hemopoietic disturbances, especially in those cases in which extensive resection for gastric carcinoma has been performed, and in which patients have survived for long periods. All such patients should be carefully observed from time to time with respect particularly to their blood-forming capacity.

SECONDARY ANEMIA

Secondary and hypochromic forms of anemia as direct results of operation undoubtedly are of much more frequent occurrence than are primary or hyperchromic anemia. The incidence may be greater than the comparatively small number of cases reported would lead one to believe, because anemia may be present to a considerable degree without giving rise to symptoms. This phase of the subject has been thoroughly reviewed by Vaughan and by various other writers. Walton encountered only six instances of anemia, all of secondary type, among 794 cases in which local resection or partial gastrectomy had been performed. Rosenthal and Abel examined the blood in 114 of Berg's cases, from six months to seventeen years after subtotal or total gastrectomy for peptic ulcer and for other conditions. They found no case of pernicious or hyperchromic anemia; in 9 per cent moderately severe, and in 5 per cent. severe anemia was observed. This anemia was not necessarily the result of the operation in all cases, in the opinion of these authors.

Such clinical experience is more in accord with the changes in the blood following experimentally produced achylia gastrica. Ivy and his co-workers have shown that following gastrectomy hypochromic microcytic (secondary) anemia occurred in a few male dogs and in all pregnant female dogs. A similar type of anemia also occurred in gastrectomized rats, pigs, and, according to Goldhamer, in monkeys. The achlorhydria was considered to be a factor predisposing to the development of anemia because it impairs the normal process of digestion as well as the assimilation of the antianemic factor.

We shall next report one of the very few cases of severe secondary anemia following gastric resection which has come under our observation.

Case 4.—A man, aged thirty-seven, came to this Clinic in May, 1924. He gave a history of gastric ulcer with hemorrhage. Nothing of significance was revealed on general examination except a tender region in the epigastrium. Except that roentgenologic examination of the stomach gave evidence of a small gastric ulcer at the incisura, laboratory tests were not significant. The concentration of hemoglobin was 80 per cent (Dare); erythrocytes numbered 4,500,000 in each cubic millimeter of blood, and analysis of the gastric content after a test meal disclosed total acidity of 40 and free hydrochloric acid of 20 (Töpfer's method). May 20, 1924, partial gastrectomy (posterior Polya) was performed. About half of the stomach was removed because of a subacute gastric ulcer situated immediately above the pylorus, on the posterior wall. The appendix was chronically inflamed, contained fecal concretions, and was removed.

In August, 1929, the patient returned to this Clinic stating that he had had no trouble with his stomach since the operation in 1924. He had not been troubled by indigestion, unless he overate or ingested too much greasy food. He complained of fatiguing easily, and of weakness. These symptoms had begun about a year before, and, at about the same time, the patient had noticed that he was becoming pallid. He was dyspnoeic and his legs ached. His tongue, he said, had been sore, intermittently, for eight months, and on two occasions it had had the appearance of raw beefsteak. Overexertion caused palpitation and tachycardia. He found it necessary to take cathartics frequently, because of constipation. Occasionally there were numbness and tingling in the fingers.

When the patient entered this Clinic the second time, the value for hemoglobin was 32 per cent; erythrocytes numbered 3,330,000 and leukocytes 6,600 in each cubic millimeter of blood. After a week, the concentration of hemoglobin was 26 per cent and erythrocytes numbered 3,060,000. Examination of blood smears gave evidence of secondary anemia of hemoglobin deficiency type. Microscopic examination gave no suggestion of pernicious anemia. Fractional analysis of the gastric content after a test meal, and after injection of histamine, disclosed absence of free hydrochloric acid. Little of consequence was revealed on general examination apart from the pallor and a palpable spleen. Because of the sore tongue, the numbness and tingling, and the achlorhydria, it was believed that dietary treatment with liver, such as is used in pernicious anemia, ought to be tried. Several weeks of this treatment failed to produce improvement. Inasmuch as good results had been obtained in pernicious anemia by the feeding of raw gastric material, it was thought desirable to try the effect of this treatment. However, the patient could not remain at the Clinic; therefore, he was sent home with directions to try fetal liver.

For about four and a half months he took the prescribed dose; also he took dilute hydrochloric acid. The concentration of hemoglobin increased from 5.5 to 7.9 gm. in each 100 c.c. of blood (photo-electrometric method; normal 15 to 17 gm.) but the number of erythrocytes per cubic millimeter of blood changed little.

Because response to this treatment was insufficient, the patient desired to try taking gastric tissue. He returned to this Clinic, was put in the hospital, and was given, daily, half a pound (0.2 kg.) of raw pork stomach in orange juice or tomato juice. He took this with little objection and with no difficulty. After three weeks in the hospital under this treatment there was little improvement in either concentration of hemoglobin or number of erythrocytes. He was then given, in addition, 20 grains (1.3 gm.) of ferric citrate three times a day. Within two weeks the concentration of hemoglobin had risen from 7.45 to 9.8 gm. in each 100 c.c. of blood and the number of erythrocytes from 4,150,000 to 4,770,000 in each cubic millimeter of blood. He was sent home to continue the use of the raw gastric material and ferric citrate. In a letter received two and a half months after the patient's dismissal, he stated that he was continuing the treatment as outlined and that he had noted considerable improvement. The concentration of hemoglobin was reported as 72 per cent, the number of erythrocytes as 5,480,000 and the number of leukocytes as 8,550 in each cubic millimeter of blood.

Whether, in this case, anemia and achlorhydria would have developed even though the patient had not undergone partial gastrectomy, of course, remains unsettled. Nor can the improvement definitely be said to have been brought about by the gastric material; it is possible that it was largely the result of the large doses of iron given. However, the combination of iron and gastric material probably should be given credit for the well marked improvement.

The above patient registered again at this Clinic, August 14, 1933. He reported that he had used ferric citrate and raw stomach until July, 1931, when he had discontinued the use of both because his blood and general condition seemed so good. In May, 1932, his blood was normal, but in December of that same year he resumed taking raw stomach and in May, 1933, resumed taking the iron. A blood count in December, 1932, revealed about 3,700,000 erythrocytes per cubic millimeter of blood. The patient reported that he had not had sore tongue, diarrhea or paresthesia. In December, 1932, a severe cold developed, and paroxysmal dyspnea supervened.

Examinations of blood made in August, 1933, revealed the following: hemoglobin, 17.8 gm. per 100 c.c.; erythrocytes, 5,130,000, and leukocytes, 9,200 per cubic millimeter of blood. The percentages of the various types of leukocytes were as follows: lymphocytes, 22.5; monocytes, 4.5; neutrophils, 69.5; eosinophils, 3.0; basophils, 0.5, and reticulated cells, 1.5. There was considerable anisocytosis and some cells gave evidence of hypochromasia. Evidence of immaturity of erythrocytes was not seen. Fractional analysis of the gastric content after a test meal resulted in determination of total acidity of 4 and absence of free hydrochloric acid. The total quantity of gastric content aspirated measured 20 c.c. Roentgenograms of the thorax revealed slight cardiac enlargement through the auricles. Roentgenoscopic examination of the stomach and anastomosis disclosed a normal gastric outline and good function of the anastomosis. By electrocardiography, the following data were obtained: cardiac rate, 60 beats per minute; sinus bradycardia; right ventricular preponderance (marked); exaggerated T wave in derivation 2; exaggerated P wave in derivations 2 and 3; notched QRS complex in derivations 2 and 3; slurred QRS complex in derivation 1; (QRS complex, in derivations 1, 2 and 3, respectively, measured 0.10, 0.12 and 0.12 second). The final diagnosis was: asthmatic bronchitis, mitral endocarditis with stenosis and regurgitation, former secondary anemia and hemorrhoids.

TREATMENT IN CASES IN WHICH ANEMIA FOLLOWS OPERATION

It is important to determine the variety of anemia that is present. The primary or hyperchromic, macrocytic type of anemia responds well to liver, liver extract or ventriculin, whereas the hypochromic, microcytic type of anemia responds well to generous doses of iron, preferably ferric ammonium citrate. This preparation of iron contains more metallic iron than do Blaud's pills, is the least astringent of the preparations of iron, and is less likely to give rise to constipation than are the other preparations. In some cases a combination of liver extract or ventriculin with iron is more effective than is iron without such biological preparations.

The diet should contain an adequate amount of vitamins and iron and should include foods which are known to be effective in the production of hemoglobin; namely, liver, kidney, giblets, peaches and apricots especially. Proper postoperative dietetic precautions may prevent or retard the onset of severe anemia.

TABLE I

Results of Examination of the Blood Seven and Eight Years After the First Operation in Case 3

Date	July 20, 1922	Sept. 27, 1922	Nov. 11, 1922	Jan. 15, 1923	Jan. 22, 1923
Hemoglobin, per cent	70	68	65	68	70
Erythrocytes, per cubic mm. of blood	3,400,000	2,780,000	1,930,000	2,480,000	3,400,000
Leukocytes, per cubic mm. of blood		7,400			

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The Results of Fat Tolerance Tests and Blood Sugar Estimations Performed on Patients Affected with Peptic Ulcer*

With a Discussion of Factors Possible in the Etiology of Peptic Ulcer

By

MAURICE A. SCHNITKER, M.D.

and

E. S. EMERY, JR., M.D.

BOSTON, MASSACHUSETTS

WE HAVE been led to determine the blood fat in patients affected with peptic ulcer because enough data has accumulated in recent years to indicate that a derangement of fat metabolism may play a part in the production or the maintenance of this disease.

Many experimental attempts have been made to reproduce peptic ulcers of a chronic type in animals, but despite numerous theories the etiology still remains obscure. The one theory about the disease which has grown steadily in importance is that ulcer is related or associated in some way with the hydrochloric acid produced by the stomach (1), (2). Acceptance of this supposition leads to one of two conclusions: *First*, is the long-held conception that ulcer results from a decrease in the normal resistance of the mucous membrane to the digestive power of the physiological gastric juice. In this group belong all the theories of etiology based on vascular disease, vascular spasm from neurogenic origin, infectious and toxic disturbances. The *second* conception is that ulcer occurs in a normal mucous membrane as the result of an increase in the destructive effect of the hydrochloric acid. Inasmuch as the stomach secretes acid of a fixed strength, as Boldyreff (3) has shown, it would seem that this increase in destructiveness, if present, must result from insufficient neutralization.

It has been the opinion of some that hydrochloric acid of a strength similar to that secreted by the stomach can destroy apparently normal tissue. Since Boldyreff (4) contends that the acidity of the gastric contents is regulated by a regurgitation of the alkaline juices of the duodenum, a high degree of gastric acidity, theoretically, could be reached by a failure of the regurgitation of alkaline duodenal contents. To determine the significance of this regurgitation, Mann and Williamson (5), and later Morton (6), studied the effect of the prevention of neutralization of the hydrochloric acid. They accomplished this by severing the duodenum from the stomach, closing one end and suturing the other end into the terminal ileum, and anastomosing the jejunum to the pylorus. This "surgical drainage of the duodenum" allowed the duodenal contents to drain into the lower reaches of the intestine. Dragstedt (2) has simplified this procedure by inserting a one-way valve into the pylorus, thus preventing the regurgitation of the duodenal contents. The success of these experiments in reproducing a lesion in animals apparently identical with that observed in man lends strong support to the idea that an unneutralized gastric juice is responsible for the development of ulcer in man.

Yet, in spite of this evidence, it is difficult to understand how this can explain all the clinical manifestations of the disease. Before this view can be accepted it must be shown that a failure of normal regurgitation occurs in patients with peptic ulcer. In order to explain the remittent nature of the disease, it must be shown that there is a failure of regurgitation during the periods of activity and that there is normal neutralization of gastric contents during the periods of healing

*From the Medical Clinic of the Peter Bent Brigham Hospital. Submitted November 25, 1934.

and quiescence. Furthermore, it is difficult to understand how those factors which are known to precipitate a recurrence of symptoms, such as emotion, infection and fatigue, act to produce a failure in the "normal neutralization" of HCl by duodenal regurgitation. Finally, it must explain the frequent tendency to seasonal relapses in patients affected with ulcer.

It would appear easier to explain many of the characteristics of the disease by a fluctuation in resistance of the mucous membrane than by the destructive effect of the gastric juice. There are many patients with ulcer who have acid readings as low as, or lower than, the so-called normal. If a gastric analysis gives an index of the secretory conditions of the stomach, many cases give no evidence that ulcer results from an increase in the destructive effect of the hydrochloric acid. Then too, the results of frequent gastric analyses do not point to any change in gastric acidity from the periods of activity to the periods of quiescence of ulcer. Since the mucous membrane normally resists the destructive effect of the hydrochloric acid and pepsin (otherwise it would not be present at all) and since unneutralized hydrochloric acid, plus pepsin, in the stomach can destroy the mucous membrane, it would appear that both the factors of resistance and of destruction must be present. No fixed point of acidity has been determined above which ulcers develop in the human or below which ulcers fail to develop. Therefore, to us, it seems reasonable to suppose that the resistance of the mucous membrane may be the deciding factor as to whether or no an ulcer shall occur. If the degree of acidity is the only factor in ulcer, one would anticipate that patients with high acid would not respond so well to treatment as would those with low acid. However, Emery and Monroe (7) have submitted data to show that if one eliminates those patients who exhibit a continuous secretion at night, the others respond equally well to treatment, irrespective of the degree of acidity and whether or no an alkaline type of therapy has been used.

As one approaches the subject from the point of view of tissue resistance, he cannot fail to be impressed by the numerous experimental studies that have reported the development of ulcers in animals when the bile is diverted from the duodenum or when the liver has been injured. Recently Schnitker and Hass (8) have covered the literature in some detail concerning the apparent relationship between the bile and the development of ulcers. The reader is, therefore, referred to their article for data and for the bibliography. These observers point out that the most successful surgical and chemical means used to produce ulcers experimentally, mostly in dogs, always have been those which side-tracked or shut off the bile from the duodenum or which have damaged the liver. Diversion of the bile has been accomplished (together with all the other duodenal secretions) by the experimental technique of "surgical drainage of the duodenum", (5), (6), or alone by Kapsinow's method (9) of anastomosing the gall bladder to the renal pelvis; both methods have been followed by the development of ulcers in a high percentage of instances. Damaging the liver by chemicals also has resulted in ulcers even when all direct effects of the substances on the mucous membrane of the stomach have been guarded against (10), (11), (12). The fact that all the best methods for the production of chronic ulcers in animals involve the hepato-biliary mechanism is too impressive to be ignored.

Further, the study of Schnitker and Hass demonstrates that there is no ordinarily demonstrable histopathologic change in the liver of patients affected with peptic ulcer, and that if there is an alteration of the biliary system associated with this disease, probably it is functional in nature. Apparently there is a disturbance of function in some cases inasmuch as McClure and Huntsinger (13), by careful analysis of duodenal contents, found that in eight of twelve patients with symptoms of "activity" of uncomplicated duodenal ulcer, the biliary fraction was "decidedly abnormal", particularly with respect to the bile acids. This observation should stimulate further study in the apparent relationship between the bile and peptic ulcer formation.

SIGNIFICANCE OF BILE IN THE CAUSATION OF PEPTIC ULCER

As yet there have been few, if any, attempts to determine in what way bile may be related to peptic ulcer. Three possibilities present themselves: *First*, that the bile serves as an essential buffer to the hydrochloric acid; this has been the most frequent explanation. However, Boldyreff (3) seems to have shown very definitely that only the pancreatic juice neutralizes the gastric acidity. He says "bile and the intestinal juice have a very small degree of alkalinity and in normal conditions do not participate in this process (viz., neutralization)." It may be stated in this connection that diversion of the pancreatic juice alone, as accomplished by Loewy (14), Berg and Jobling (15), Berg and Zucker (16), and Berg (17), has led to a smaller incidence of ulcer than has diversion of bile. These findings suggest that the development of ulcer following the diversion of these secretions depends upon some factor other than a decrease in the neutralization of the gastric juice. However, these observations could be explained by Mellanby's observation (18) that the entrance of bile into the duodenum of cats, under suitable conditions, causes a copious secretion of pancreatic juice. In contradiction to this finding, Dragstedt and Woodbury (19), working with dogs, were unable to obtain results similar to those of Mellanby. Further studies must be made before these questions definitely may be answered, but to the present it has not been established that the cause of peptic ulcer lies in an insufficient neutralization of the gastric acidity.

A *second possibility* is that *diversion of bile* causes a loss of some substance to the body, the lack of which substance results in an increased susceptibility of the mucous membrane to the damaging effect of hydrochloric acid. Berg and Jobling (15) suggest that such a substance may be the biliary mucus.

The *third possibility* is that a disturbance in the metabolism of fat occurs which in turn leads to the development of ulcers. Fats are "an essential constituent of cells and cell membranes, and although little is known about their behavior in the tissues, there is sufficient evidence that a change in the metabolism of fat may result in important bodily effects" (20). Macleod (21) states that "lecithin is an extremely important constituent of cells and seems to be the intermediate stage in the utilization of neutral fats by protoplasm". Tashiro and Schmidt (22) have suggested that certain fractions of the cell phospholipids may be concerned with the protection of its own tissue against proteolytic action and that of other ferments. Recent work indicates that the portions of the intestinal tract which have somewhat higher lipid contents exert greater resistances to the destructive effect of hydrochloric acid. Sperry (23) has reported that the amount of lipids is somewhat greater in the cells of the upper intestinal tract than it is caudad. When McMaster (24) performed gastro-enterostomies in dogs at progressively lower levels from the duodenum to the colon, inclusive, he found that the lower in the intestinal tract the anastamosis was made the greater was the frequency of post-operative ulcers. Finally, in connection with the idea that a disturbance in fat metabolism may play an important part in the etiology of peptic ulcer, we have the statement of Michaelis (25) as expressed in the Harvey lectures: "Why does not the acid pepsin-containing gastric juice digest the wall of the living stomach itself? It seems to me that this problem no longer involves any difficulties. It is virtually certain, from a histological aspect, that the acid and the pepsin, though produced in the same glands, are not produced in the same cells. The mixing takes place only in the cavity of the stomach. Now the superficial cell membranes, which regulate the permeability of any cell, seem to consist of some lipoid substance. Obscure and equivocal though this term may be, at least it is not a protein which may be subject to the action of pepsin. So, the membranes of the mucosa being indigestible, and certainly also impermeable for a molecule of such a large size as that of pepsin, will prevent the interior of the cells from being digested as long as the membrane is intact."

On the basis of Michaelis' hypothesis, anything which disturbed the lipoids in the cell membrane might lead to peptic ulcer. One is led, naturally, to consider whether the fact that ulcers develop in animals if the bile is diverted from its usual course may be related to an effect upon the lipoid content of the cells.

This conception leads to numerous possibilities in connection with the development of peptic ulcer in man. Because the bile may bear a close relation to ulcer, further study of this secretion from both a quantitative as well as a qualitative point of view would seem to be indicated. We have little knowledge of the functions of the bile in addition to its importance in the digestion and absorption of fat; it is a complicated substance and probably has many qualities and exerts many effects about which, at present, we are ignorant (26). We do not know what effects, if any, bile exerts after it is reabsorbed from the intestine. In addition to its function of aiding fat digestion, bile is thought to stimulate peristalsis and is known to serve as a medium for the excretion of various substances, as toxins or metallic poisons. It is conceivable that qualitative changes can occur in the bile which are not recognized at present but which may have far-reaching systemic effects. Hence, the investigation of the cause of peptic ulcer should include careful studies of the bile as well as of the tissues of the stomach and the duodenum. As the first approach to this problem, we have analyzed the blood fat in patients with ulcer.*

STUDIES OF BLOOD SERUM FAT IN PEPTIC ULCER PATIENTS

A study of this kind is limited to what may be termed "intermediary fat metabolism"; this includes a qualitative and quantitative estimate of the various fractions of the blood-fat at a given time. A study of the total lipoids does not reveal the distribution or concentration of fats in the various body cells, but if one analyzes the blood at intervals following the ingestion of a fat meal, he may obtain an idea of the rate of absorption of fat from the intestinal tract and also the rate at which the lipoids leave the blood stream.

MATERIAL.

For this study we selected twenty patients whose ulcers presented various degrees of activity. Some were having periodic ulcer pains, others were in the second and third weeks of ulcer treatment and were or were not experiencing pain. Certain subjects were examined when free from all distress, at times when roentgen observations demonstrated only duodenal deformity without evidence of ulcer activity. Most of the patients were affected with duodenal ulcer, only three of them having gastric lesions. Nineteen subjects definitely were ulcer cases, their histories having presented typical symptoms and definite craters having been revealed by X-ray at some time during their digestive upsets. One patient who had symptoms suggestive of ulcer is in-

*Since writing this paper, the work of Jergeson and Simonds (Jergeson, P. H., and Simonds, J. P. The Blood Lipase in Patients with Peptic Ulcer. Its Relation to Hepatic and Pancreatic Disease. *Journ. Lab. and Clin. Med.*, 19: 1054; 1934) has come to our notice. These investigations indicate an increase in an olive-oil-splitting enzyme in 38 of 50 patients affected with a peptic ulcer.

cluded, although by appropriate and careful examinations, only a gastritis accompanied by thickened *rugae* could be demonstrated.

For a *control group*, we selected ten normal, healthy individuals whose ages ranged from 23 to 40. Among these subjects, there were several who were rather obese and several somewhat thin. In making blood-serum fat estimations, the reason for selecting the two types of persons is obvious.

Certain factors were kept constant in both groups, ulcer patients and controls. Each individual tested received 90 to 100 grams of fat *per diem* for two days preceding the tests. Smoking was kept at a minimum. A hemoglobin and a red blood cell count were performed on each individual so that correction could be made for any increase of blood fat in the presence of anemia (27). As there were no hemoglobin determinations below 80 per cent (Sahli) or red cell counts lower than 4.20 million, no corrections were found necessary.

METHOD

The Rückert (28) *hemolipokrit technique*, as modified by Herrmann (29), was used in making the fat determinations. Both Rückert and Collins (30) have demonstrated that this method is sufficiently accurate for clinical purposes.

The modified Rückert technique is a volumetric determination of the total fat content of the blood serum and is identical in principle with the Babcock and the Gerber methods employed for estimating fat in milk. The method consists of adding acid and alcohol to blood serum. The 70 per cent sulphuric acid causes a change of the serum-proteins by hydrolysis from the colloidal state to one of molecular dispersion. This allows for the liberation of fats in amyl alcohol; these may be separated by centrifugalization and then can be measured volumetrically in a specially constructed vessel, equipped (Rückert hemolipokrit) with a graduated scale. For a description of the technique, the reader is referred to the communications of Rückert and of Herrmann.

The first specimen of blood was drawn after the subject had fasted for 15 hours. Then he ingested 500 c.c. of 20 per cent cream (equivalent of 100 grams of fat). Blood samples were drawn from the antecubital vein at intervals of 2, 4 and 6 hours. In a few cases, the test was run for 9 hours instead of 6, but because no significant differences were observed at 9 hours, most of the subjects had the 6-hour tolerance test.

The only complaint, apart from some individuals disliking the being without food for nearly 24 hours, was a feeling of discomfort in the abdomen, experienced in several of the control cases. We attributed this sensation to gastric distention due to the ingestion of 500 c.c. of fluid. In no instance, was there pain from 9 A. M. (the time the cream was taken) until 3 P. M., at the time when the test terminated, although some of the patients had experienced pain the day prior to the test.

The whole blood, collected in 6 c.c. quantities in small clean test tubes, was allowed to clot and then was centrifugalized for five minutes at 2,000 R. P. M. in order that it would yield the maximum amount of serum with a minimum demulsification of the fats (29).

Our experience agrees in general with that of Collins, namely, that the readings for the fractions of neutral fats, free fatty acids, cholesterol and cholesterin esters (which are supposed to separate immediately upon centrifugalization) were quite inconstant.* However, when these readings were recorded, the tubes allowed to stand at room temperature for 14 hours, again centrifugalized and the second reading (the phosphatid fraction) was added to the first (to give the total fats), the figures in duplicate tubes agreed satisfactorily. Since we wished to determine only whether the patient with an ulcer had a different type of fat tolerance curve from that of the normal individual, the method appeared to be adequate.

RESULTS

The character and the concentration of most lipoid constituents in the blood serum differ from those of the blood cells. The changes occurring in the blood following the ingestion of fat are quite variable (particularly cholesterol), a change depending upon the nature of the food fed (31) and the time which elapses before the blood is taken following the fat meal (32). On the other hand, the proportion of cholesterol esters usually increases following the ingestion of fat. A rise in the phosphatids accompanies the rise of the total fat. The fractionation of the fatty acids has been of no value so far in the diagnosis of disease. Consequently it was felt that a study of the total lipoids of the blood serum would yield the most satisfactory information.

Although starvation usually causes a hyperlipemia affecting all the lipoid constituents of the blood (33), this is apparent only after long periods of time and usually not before 24 hours. Blood fat is not appreciably influenced by the 15-hour fast as carried out in our work. The fasting level of total lipoids in most of the patients with ulcer varied between 600-800 milliliters per cent; that for the normals ranged between 650-800 milliliters per cent, a level slightly higher than that obtained by Herrmann (29).

There was considerable variation in the individual curves for the patients affected with ulcer; this is brought out in *Chart I.* In 17 of the 20 cases, the fat level in the blood rose within the first two hours following the ingestion of the meal. The average rise was 120 milliliters per

*After this work was completed, Dr. Louis Herrmann has told us that, since the procedure is based on the principle of hydrolysis in which the time factor is very important, the difference of several minutes in filling four tubes (convenient in the shaking apparatus) will readily account for such a discrepancy. It is advisable, then, to run only two tubes at a time as a check.

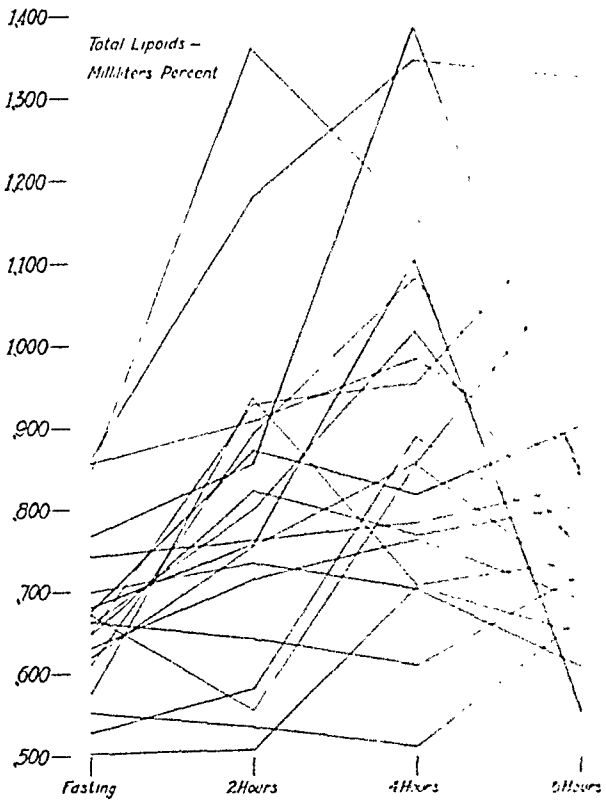


Chart 1. Illustrating the Variability of Fat Tolerance Curves in patients with Peptic Ulcer.

100 c.c. of blood. In 13 patients, it continued to rise on an average of 200 milliliters per cent. between the second and the fourth hours, and in seven it dropped, an average of 90 milliliters per cent. In 12, it declined after the fourth hour, though not necessarily in the same individuals in whom it had been elevated at the end of four hours. In eight, it rose between the fourth and the sixth hours. In most of the cases, the curve had returned to the fasting level in six hours. This variation in the type of individual curves occurred also with the control cases. As it is impossible to compare the trend of so many curves, *Charts II* and *III* have been prepared for the sake of clearness. They show the curves which include the highest and the lowest figures recorded and the average curves for the 20 patients with ulcer and also for the 10 controls.

A comparison of Charts II and III shows that the average level for the patients with ulcer approximately was 100 milliliters per cent lower than it was for the controls. However, it seems unlikely that this difference in level has any significance because the type of the two curves essentially was the same and the fluctuation between the individual cases was so marked.

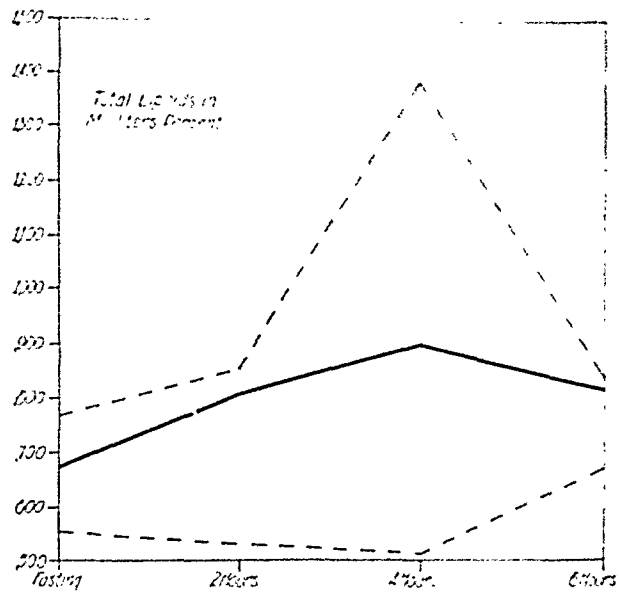
Chart 2. Fat Tolerance Curves in patients with Peptic Ulcer. The broken lines show the maximum and minimum results recorded. The solid line is the average for 20 patients.

BLOOD SUGAR ESTIMATIONS

There has been considerable interest of late in the behavior of the blood sugar in patients affected with peptic ulcer. Recht (34) believes that the administration of grape sugar heals an ulcer and tends to prevent its recurrence. Certain writers, as Van den Bergh and Van Heukelom (35), found a delayed type of blood sugar curve in ulcer cases. On the other hand, similar studies carried out by Scherk (36), Friedenwald and Grove (37) and Jankelson and Rudy (38) have shown no deviation from the normal. Enoch-son (39) has described what he terms a "hyperglycemic area", a standard estimated on the relation between time and height of the blood sugar; this, he found, to be increased for patients in whom ulcers were active.

Therefore, we considered it to be of interest to determine the blood sugars in our series of patients in order to learn whether or no we could confirm the findings of other observers and to note whether or no there could be an association between the blood sugar and the blood serum fat, should the latter show a change from usual values.

Normally, the blood sugar presents little change after a meal rich in fats. After feeding to dogs olive oil in 50 c.c. quantity, Li (40) observed no essential variation from the normal in the type of blood sugar curve. In studying the sugar content of the blood in normal and undernourished individuals, Brown (41) noted no difference in the absorption of carbohydrate, whether large amounts of fat had been fed with sugar or the sugar alone was given.



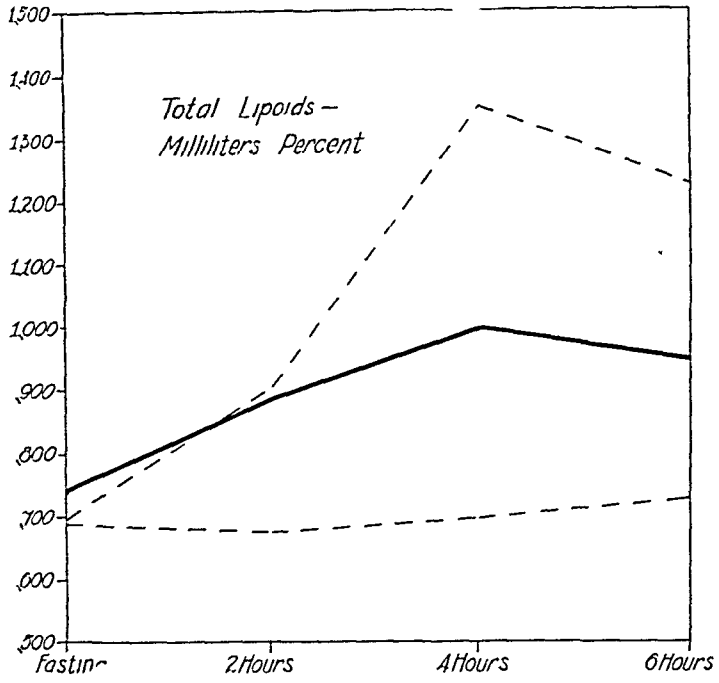


Chart 3. Fat Tolerance Curves in normal individuals. The broken lines show the maximum and minimum results recorded. The solid line is the average for 10 persons.

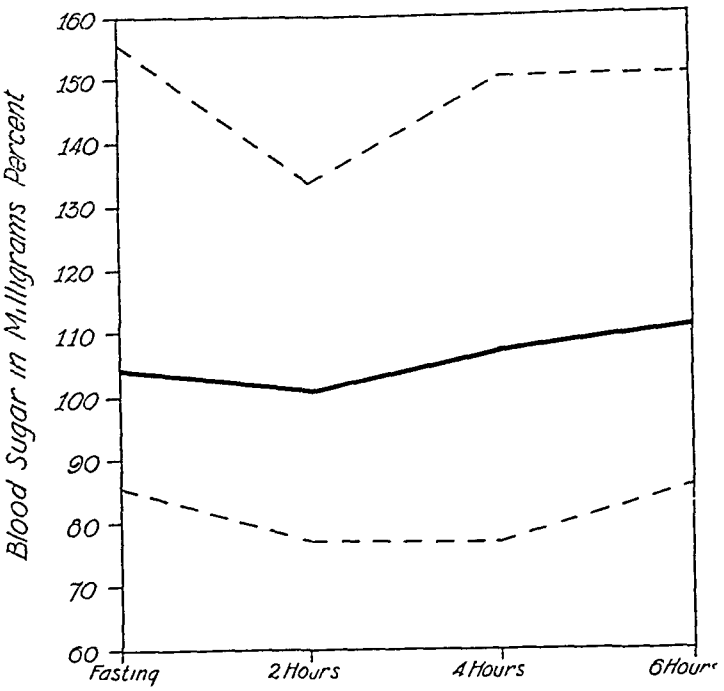


Chart 5. The blood sugar levels in normal individuals after a meal of 100 grams of fat. The highest and lowest curves are shown by the broken lines. The solid line is the average for 7 persons.

Sufficient blood was drawn from 15 patients with ulcer and from seven of the control individuals to make both the fat and the sugar determinations. The results are shown in Charts IV and V. These also record the maximum and minimum fluctuations for individual curves together with the average for the group.

It will be seen that the average for the ulcer cases showed a slightly different type of curve from that of the controls. No significance could be attached to this, however, in view of the wide variations apparent in the individual curves. We concluded from these observations that there is no essential variation from the normal in the behavior of the blood sugar following a fat meal in patients with a peptic ulcer.

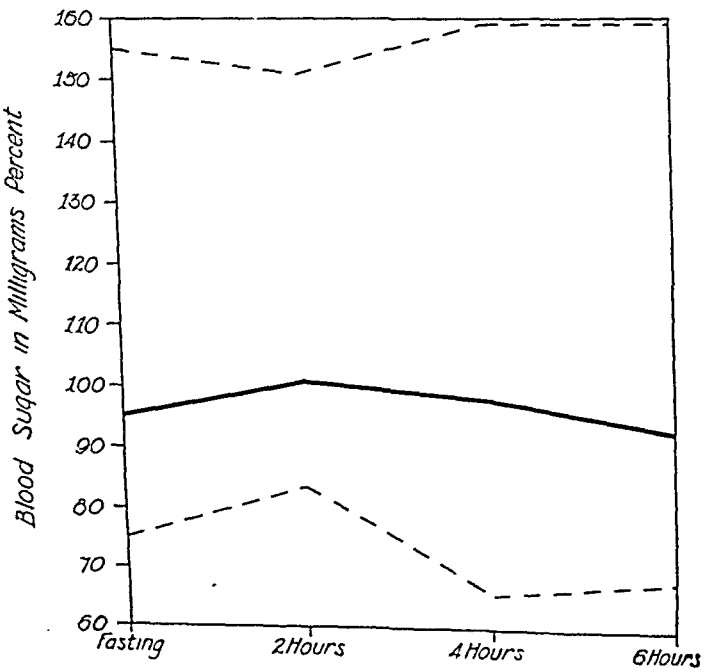


Chart 4. Blood sugar levels following the Ingestion of 100 grams of fat in patients with Peptic Ulcer. The highest and lowest curves are shown by the broken lines. The solid line is the average for 15 patients.

SUMMARY AND CONCLUSIONS

Measures that include diversion of bile from the duodenum or injury to the liver have been found to produce chronic peptic ulcers in dogs. The possible *rôles* of bile in the prevention of ulcers are discussed. That loss of bile from the duodenum may result in lowered tissue resistance because of a disturbed fat metabolism is considered.

On this basis, we have made a study of fat tolerance tests done on 20 patients affected with peptic ulcer. These curves showed no significant differences from those of a group of 10 normal persons. These data seem to preclude any gross disturbances in digestion, absorption and metabolism of fat in such patients. However, they do not rule out the possibility that disturbances of fat may be present which cannot be recognized by the Rückert *hemolipokrit* method, used in this study. Comparative studies of the quality and nature of the lipoid constituents of cells of the ulcer-bearing areas in patients with and without ulcer, might throw further light on the subject.

Over a six-hour period, no differences could be observed in the blood sugar curves of patients with peptic ulcer compared with normal individuals, following the ingestion of 100 grams of fat.

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An Instance of Gelatinous Carcinoma of the Duodenum*

By

J. ALLEN WILSON, M.D.

and

JOHN F. NOBLE, M.D.

ST. PAUL, MINNESOTA

FREQUENCY, LOCATION AND PATHOLOGIC TYPE OF DUODENAL MALIGNANCY

CARCINOMA of the duodenum rarely is found at autopsy and is much less frequently diagnosed before death. Statistics assembled by Brill (1) in 1904 from reports, by various authors, on 24,160 cases of carcinoma of all organs, give carcinoma of the small bowel as 2.3 per cent of all carcinomas of the intestines. Other figures give carcinoma of the duodenum as only 0.3 per cent of all intestinal cancers. Kellogg (2) states that nearly one-half of all small bowel malignancies are duodenal. The majority of cases of duodenal carcinoma occur in the second portion, in the vicinity of the ampulla of Vater, Geiser (3) finding 51 in this location compared with 11 in the parapyloric and nine in the pre-jejunal segments. Kellogg (2) states that 22 per cent occur in the first part of the duodenum, 66 per cent in

*From the Medical and Pathological Services of Ancker Hospital and the Departments of Medicine and Pathology, University of Minnesota.

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the second, and 12 per cent in the third section. In a series of 15 cases from the Mayo Clinic (4) six were in the supra-ampullary, six in the ampullary, and three in the infra-ampullary areas of the duodenum.

In the cases of carcinoma arising from the first or the supra-ampullary portion of the duodenum, the malignancy has been recorded in 10 cases mentioned by Ewing (5) as having developed on the base of or following a duodenal ulcer. Whether this is merely coincidental is a question which has been argued many times. Letulle (6) described his specimen as developing within the crater of an ulcer. Ewald (5) found a carcinomatous area in the scar of a healed ulcer. Geiser (3) collected six cases of duodenal cancer following ulcer but he thought that the relationship in the duodenum of scar-formation to cancer has been overemphasized, for, he suggested, scars can be formed secondarily to ulceration in a carcinoma. Meyer and Rosenberg (7) in a review of the literature, state that it is their belief that resection of more duodenal ulcer scars would reveal more unrecognized carcinomas of the duodenum than commonly recorded but that correlation between the two is difficult and the two lesions may occur simultaneously. Hinton (8) emphatically states that, due to the frequency of duodenal ulcer and the rarity of duodenal carcinoma, clinically one can disregard the possibility of a duodenal ulcer ever undergoing malignant transition. The cases so reported, Hinton feels, were in all probability carcinoma *de novo*.

The pathological findings vary in the cases reported in the literature. Various writers mention the possibility of colloid degeneration but to our knowledge, this statement is based on the one carefully reported case of Letulle (6). Kellogg (2) says "the carcinoma may be scirrhous, medullary, or colloid". Necrotic changes, with ulceration, may occur. Geiser (3) states that microscopically the tumors resemble other bowel carcinomas usually with cylindrical-celled carcinoma arising from Lieberkühn's glands. No proof exists for their described origin from Brunner's glands. There is a great tendency to metastasis to the liver and lung but seldom to the peritoneum. Metastatic glands may compress the common bile duct. No brain metastases were found in Geiser's series. Brill (1) described most of these tumors as being of the cylindrical-celled variety showing a glandular type of adenocarcinoma. Some may be medullary, others scirrhous. "When the cells of the cylindrical-celled carcinomata of the duodenum undergo so-called mucoid or colloid degeneration, they give rise to the gelatinous or colloid carcinoma of the duodenum." All forms are subject to retrogressive or necrotic change, whereupon softening and ulceration occur. (No data are given by Brill on the frequency of colloid degeneration.) Ewing (5) mentions Letulle's case of colloid carcinoma and states that most duodenal carcinomas are cylindrical-celled adenocarcinoma or alveolar carcinoma. Three necropsy specimens, in the Mayo Clinic (4) report, varied microscopically from a fairly well-differentiated type of carcinoma with irregular acinous structures lined by high columnar cells and intertwined with connective tissue strands to one less differentiated, showing but a few gland-like structures and marked by areas of degeneration and local infiltration with lymphocytes. Of their 15 cases, two were large malignant papillomas and the remainder stenosing adenocarcinomas. Mateer and Hartman (9) described two unusual cases of combined squamous-cell and adenocarcinoma originating in the ampulla of Vater and the common bile duct respectively. Geiser (3) reported one case near the papilla of Vater with fatty degeneration of the tumor cells.

Letulle (6) has described very carefully a case of colloid carcinoma of the first portion of the duodenum in a patient of 55 years. The patient had been treated twice for duodenal ulcer and had partially recovered. On admission the last time, cachexia was marked, vomiting was incessant and a mass was palpable in the lower, right epigastric area. At autopsy, a large simple ulcer of the duodenum was found toward the center of which was a more recent colloid carcinoma. The calibre of the duodenum was greatly dilated cephalad to this mass, and the pylorus was gaping. A 2 cm. strip of the normal duodenal mucosa separated the mass from the pylorus. Below, the mass reached, but did not destroy, the ampulla of Vater. The pancreas was atrophied and had only a duct of Santorini, with no connection with the common bile duct. No carcinoma was found in the head of the pancreas. Microscopic study of the tumor showed a colloid carcinoma. The epithelial cells were of monstrous size and had invaded all the layers of the intestine. Many of the cylindrical cells were engorged with enormous cystic masses of mucus. The old ulcer had destroyed the layers of the bowel at that point. On the superior and inferior borders, it had a large fibrous surface with a cancerous center.

CLINICAL EVIDENCES OF DUODENAL CANCER

The symptoms of duodenal carcinoma depend on its location. If in the first portion, the diagnosis is rarely possible of differentiation from that of obstructing carcinoma of the pylorus. *Pain* usually occurs one to four hours after meals, and rarely is severe. Eusterman *et al* (4) mention flatulence, pain or distress after eating, *retention type of vomiting*, dehydration, and toxaemia as majors symptoms. *Jaundice* in their cases, except as a terminal symptom, was rare even in the ampullary carcinomas. However, nearly all other writers, especially Graham (10), describe jaundice of an intermittent type, as typical of peri-ampullary carcinoma. *Fever* accompanies the jaundice. Some writers (9) emphasize the importance of investigating unexplained *occult*

blood in the stools; this is present usually in these cases. Also persistent *failure to obtain bile* on repeated duodenal drainage, points to a malignant obstruction of the lower biliary tract (Clement Jones). Infra-ampullary carcinoma gives cachexia plus symptoms of a duodenal ileus or obstruction, with vomiting of large amounts of bile-stained fluid. *Free hydrochloric acid* has been absent or below normal in the cases examined. Most authors find the tumor more common in males of an average age of 52. Death usually occurs in 10 to 12 months after onset of symptoms.

CASE REPORT

The patient was a white, female, age 60, who was first seen in the Ancker Hospital dispensary in April, 1931, at which time she was complaining of pain in her shoulders and arms. This was diagnosed as rheumatic infection and was treated as such. She was again seen in the Ancker Hospital dispensary in January, 1933. After several dispensary visits she was admitted to the hospital.

The patient traced her present trouble to October, 1932, at which time she developed a severe upper respiratory infection associated with coughing, discharge from the nose, and general malaise. Following this, she had severe pain in the shoulders and arms which she described as a "neuritis". A phlebitis in the leg veins followed the neuritis. She was well during the first part of December, and then developed a bronchitis with severe coughing and sore throat. Considerable dyspnea was associated with this attack. The patient stated that she has suffered from "bronchitis" every winter for several years. After Christmas (1932) she began eructating a bitter, brown material after meals. She was able to retain only liquid nourishment; all solid foods taken were vomited. Shortly after this, there appeared a pain in the epigastrium which was aggravated by eating; this was a dull aching pain and was not transmitted. The patient was able to retain liquid nourishment until the early part of February, 1933. From this time she could retain practically nothing taken by mouth. It was this condition which brought her to the dispensary.

Her *past medical history* revealed that she had had some epigastric distress (not pain) at intervals for several years. This was accompanied by a sense of epigastric fullness occurring one-half to one hour after eating. It was partially relieved by soda, (½ to 1 testspoonful). A fat intolerance had been present for many years. No sharp pain in the abdomen ever had been experienced. The patient had typhoid fever and pneumonia in 1900. Septicemia, following childbirth, occurred in 1914. Some operation (type not known) had been performed on the uterus in 1903. A bilateral mastoidotomy was done in 1916. The patient had had occasional headaches and frequent attacks of vertigo following that operation. Her cardio-respiratory history revealed that she had severe dyspnea on exertion (she weighed over 260 pounds). No orthopnea had been noted. Edema of the ankles and legs had been attributed to varicose veins. A chronic cough was present but there was no hemoptysis. The menopause occurred at the age 50. The patient had borne three children who are alive and well. Two sons had had tuberculosis. One sister died of carcinoma.

On *physical examination* the patient was a very obese, elderly, white female, apparently suffering no acute pain. Her weight, which had been 267 pounds (December 20, 1932), was now (February 21, 1933) 240 pounds. The pupils were slightly contracted, and reacted sluggishly to light and accommodation. There were mastoid operative scars on each side. The mouth was edentulous; the tongue normal. The breasts were pendulous and large, with no palpable masses. There was no lung pathology. The heart tones were normal except for a muffled systolic murmur heard best over the mitral area. The blood pressure was recorded on two occasions as 88 systolic and 46 diastolic, and 112 systolic with 68 diastolic. The abdominal fat was pronounced despite the reported loss of weight. There was a suprapubic midline scar, and the navel had been removed. There was also a transverse scar eight inches long, in the lower one-half of the abdomen associated with ventral hernia the size of an orange, near the scar and slightly to the right of the midline. This was reduced with difficulty. Some tenderness, but no rigidity was elicited over the entire upper abdomen, it being most marked in the epigastrium. The liver and spleen could not be palpated at this time, but later the edge of the liver was located three finger-breadths below the right costal margin in the right mid-clavicular line. Moderate edema of the legs with numerous large varicose veins was present. Brown, pigmented areas evidently due to previous varicose ulcers were noted. The patellar reflexes were not elicited. The bicep reflexes were normal.

The patient's temperature on admission was 100 degrees F.; it remained between 99 and 101 degrees until the last few days of her stay in the hospital, when it became normal.

The woman's *clinical course* during the 14 days she was in the hospital was marked by repeated emesis of all foods and most liquids taken by mouth. The stomach was aspirated on several occasions and at one time 1,700 c.c. of fluid were removed. She complained of a constant dull epigastric pain. The fluid vomited was thin and dark yellow or green in color.

A *mass was indefinitely palpated in the epigastrium* just prior to the patient's death. Arrangements were being made to give a blood transfusion in preparation for an exploratory laparotomy, but on March 7 the patient died suddenly.

Laboratory findings were as follows: *blood examination* revealed hemoglobin 68 per cent (Sahli), erythrocytes 3,920,000, leukocytes 9,350. A differential count showed 82 per cent polymorphonuclear leukocytes, 16 per cent lymphocytes and 2 per cent monocytes. The blood urea nitrogen on February 27, 1933, was 49 mgm. per 100 c.c.; blood creatinine was 2.8 mgm. *The gastric contents*, after an Ewald meal, contained no free HCl and 30 total acid. Digestion was good; lactic acid and Boas-Oppler bacilli were present. *Urine examination* revealed a clear amber fluid with sp. gr. 1.014 and 3+ albumen. No sugar was present. Occasional hyaline and granular casts and a few leukocytes were seen.

An *X-ray examination* was attempted on February 20, 1933, just prior to the patient's admission to the hospital. The report was as follows: "Patient is too obese for satisfactory X-ray examination. Fluoroscopic examination shows complete retention of the motor meal with what appears to be a constant deformity of the distal end of the stomach. A follow-up at 24 hours shows only a very small amount of barium in the intestinal tract, the remainder of the barium being in the stomach. *Impressions:* obstructing lesion at the outlet of the stomach."

The *clinical diagnosis* made was "carcinoma obstructing the pylorus."

AUTOPSY FINDINGS

Gross Pathology: At autopsy, the body very obese. There was, however, evidence of a rather marked loss of weight. The external examination of the body revealed nothing of note save for the operative scars above mentioned in the physical examination.

The principal findings of interest at autopsy were those associated with the duodenal tumor. When the abdomen was opened, a large mass was palpated in the region of



Fig. 1. Gross specimen of gelatinous carcinoma of the duodenum, showing the infiltration of the duodenal wall with the sharp demarcation at the pyloric ring. The tumor mass also is seen bulging into the antrum of the stomach.

the duodenum and the head of the pancreas. (Fig. 1.) The duodenal wall was thickened and indurated and measured 1.5 cm. This tumor infiltration was circumferential and involved the duodenum for a distance of 5 cms. distal to the pyloric ring. It was sharply demarcated at the pylorus and fairly sharply demarcated distally. The tumor did not involve the ampulla of Vater. The surface of the duodenal wall after cutting, was gelatinous in appearance; the mucosal surface appeared to be intact save at a point just distal to the pylorus where there was a punched-out ulcer 1 cm. in diameter. This ulcer had raised edges and a crater 6 mm. in depth. There was definite obstruction at the pyloric ring, and moderate dilatation of the stomach. The tumor had extended through the duodenal wall in the region of the head of the pancreas where it largely replaced the pancreas and widened the duodenal loop. The mass in this region was so large that it encroached upon the stomach in the region of the antrum. The stomach wall was infiltrated from the serosal side and the gastric mucosa showed a small, pressure ulcer over the region of the mass. The mass was rounded and well defined from the pancreatic tissue. There was no gross evidence that the tumor had arisen from the gastric mucosa or the pancreas; unquestionably it had its origin in the duodenum. The ulcer of the duodenum occurred in an area composed entirely of tumor tissue and it was impossible to determine whether it represented simply an area of ulceration in the tumor, or a pre-existing peptic ulcer of the duodenum. The lymph nodes in the region of the celiac axis were enlarged and measured 1 to 3 cms. in diameter. They were completely replaced by tumor tissue and their surfaces, after cutting, had the same gelatinous appearance as had the primary tumor, but there was, in addition, considerable hemorrhage into the lymph tissue, giving it a definite reddish color. The liver weighed 4,670 grams. Its surface was covered with numerous, raised hemorrhagic nodules, varying from 1 to 5 cms. in diameter. The surface of the liver, after cutting, was found to contain innumerable metastatic nodules, which were well defined from the liver tissue. In general they were round and had the same hemorrhagic appearance as had the metastases in the lymph nodes. The liver was largely replaced by this metastatic tumor. Situated in the main branch of the portal vein, there was a thrombotic mass 2 cm. in diameter which was very loosely attached to the intima of the vein. It did not completely occlude the lumen and there was no evidence of infarction of the liver tissue. A small radicle of the portal vein in the substance of the liver was encroached upon by a tumor nodule and also showed an adherent thrombus opposite the area of tumor invasion of the vein.

An extensive, bilateral bronchopneumonia also was noted which appeared to be a contributory cause of death. The heart weighed 435 grams. It showed moderate left ventricular hypertrophy and the mitral valve exhibited a single, friable, thrombotic vegetation 2 mm. in diameter.

The anatomic diagnosis was: gelatinous carcinoma of the duodenum with metastases to the liver and celiac lymph nodes, and direct extension into the pancreas and stomach; bilateral bronchopneumonia; portal thrombosis, and acute bacterial endocarditis of the mitral valve.

Microscopic Studies: Sections through the wall of the duodenum (Fig. 2), showed a typical picture of a gelatinous carcinoma. The mucosa was largely destroyed by tumor infiltration and the small islands remaining had undergone *post-mortem* digestion. The tumor was made up largely of a loose connective tissue stroma, the interstices of which were filled with a stringy, mucinous material. Scattered throughout this material, the degenerating tumor cells were seen singly, and in irregular clumps. In only small areas of the tumor, was there any attempt at gland formation. In these areas, the lumina of the glands were distended by mucus. The mucinous material undoubtedly had its origin from the epithelium, for throughout the tumor, numerous epithelial cells were seen to be distended with mucin so that they took on a signet ring form. (Fig. 3.) Degenerating cells of this type, discharging their contents, accounted for the large amounts of the mucinous material infiltrating the tissue. The tumor cells were pyknotic. Mitotic figures were numerous. The entire thickness of the duodenal wall was found to be infiltrated, the muscle bundles being widely separated by the tumor tissue. The entire wall of the ulcer of the duodenum was made up of tumor tissue, leaving nothing to indicate an antecedent primary peptic ulcer. There was no actual infiltration of the pancreas. The pancreatic tissue was simply pushed aside and replaced by tumor.

The metastases in the liver largely were necrotic and infiltrated by hemorrhage. At the margins of the necrotic masses, irregular clumps of tumor cells were seen. These cells were somewhat larger and better preserved than were those of the primary tumor, and the gelatinous character largely was absent though occasional cells of the signet ring type were seen.

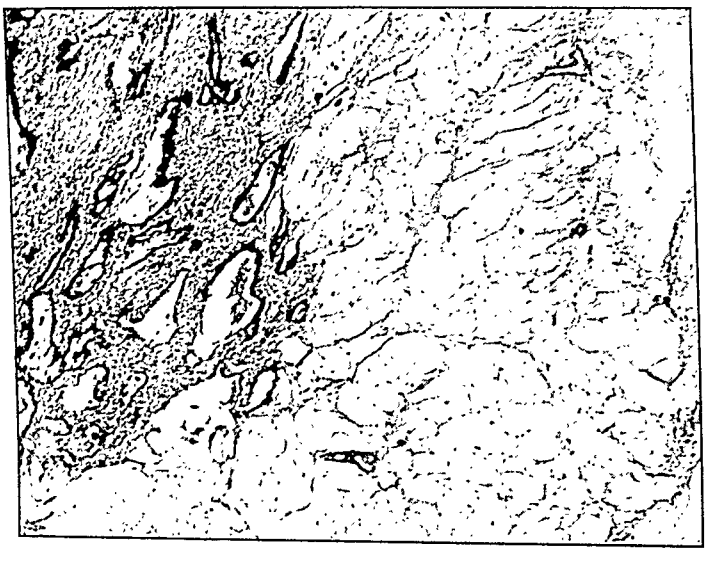


Fig. 2. Microscopic section of gelatinous carcinoma of the duodenum, showing the gelatinous tumor infiltration of the entire duodenal wall.



Fig. 3. Microscopic section (high power) of gelatinous carcinoma of the duodenum, showing the individual epithelial tumor cells distended with mucus.

DISCUSSION

Pathologically, this tumor must be classified as a gelatinous carcinoma of the first portion of the duodenum. It seems unusual that so few cases of gelatinous carcinoma are reported in this location because of the abundant mucus-forming cells in the crypts of Lieberkühn, and because of the mucous glands of Brunner deep in the wall of the duodenum. In this case, no evidence could be found to prove whether the tumor had originated in the mucosa itself or in Brunner's glands. There seems, however, no doubt that the gelatinous material had its origin from epithelium and not from the stroma of the tumor.

This patient was diagnosed, clinically, as having an obstructing carcinoma of the pylorus, as has usually been the case in para-pyloric carcinoma of the duodenum. The X-ray findings, when a tumor is located as was found in this patient, seldom, if ever, can establish the true diagnosis. This subject was so obese that accurate *antemortem* palpation of the tumor was not possible.

The treatment of carcinoma of the duodenum is, of course, resection, if the diagnosis can be made early, accompanied by cholecystgastrostomy, when obstructive jaundice is present. When the tumor has extended to other organs, a palliative gastro-enterostomy is justifiable, after proper preparation of the patient.

CONCLUSIONS

1. A case history, with the pathological findings of gelatinous carcinoma of the duodenum is presented.

2. Gelatinous carcinoma of the duodenum rarely is reported, but its possibility occasionally is mentioned. The instance previously described in the literature which the authors have discovered, is cited.

3. In the patient here reported, as is usually the case when carcinoma involves the first portion of the duodenum, the lesion could not be satisfactorily differentiated clinically from carcinoma primarily obstructing the pylorus.

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ABSTRACTS

BALDRIDGE, C. W.

The Relationship Between Antisyphilitic Treatment and Toxic Cirrhosis. J. Am. Med. Sc., 188:685-690, November, 1934.

The author propounds the question as to whether, in syphilis, the therapeutic agents, namely, mercury and arsenic, may produce a toxic cirrhosis of the liver and further divides the question to include the possibility of a non-syphilitic liver developing cirrhosis when exposed to an antisyphilitic agent. To support his claims, he quotes thirty-six cases of cirrhosis of the liver of which twelve had had antisyphilitic treatment, namely, arsphenamine or neoarsphenamine. Clinically, none of these patients had evidences of liver disease before treatment was begun. Four patients came to necropsy of which three showed a toxic type of cirrhosis which was assumed to be a result of a previous acute yellow atrophy. Of these three, one of them was an individual who had not had syphilis but had been exposed to long, continued antisphilitic treatment.

M. G. Vorhaus, New York, New York.

SECTION II—*Experimental Physiology*

The Applied Physiology of the Gastro-Intestinal Innervation

Certain Selected Topics*

By

A. C. IVY, Ph.D., M.D.†
CHICAGO, ILLINOIS

THE subject of this lecture was chosen because of its general applicability to the topic under consideration during this fortnight of study. In view of the time allotted to the lecture the subject matter has been selected and will be presented in synoptic style. The topics selected pertain primarily to disturbances of motor activities, since disturbances of motility more frequently cause symptoms than disturbances of secretory activity.

All portions of the gastro-intestinal tract are intimately correlated by extrinsic and intrinsic nervous mechanisms and humoral agencies. Thus, in many diseases of the gastro-intestinal tract, we must think of the tract as a functional unit, and not solely of the viscus in which an organic lesion or disease is located.

First, I should like to discuss briefly *the relation of the cerebral cortex to the autonomic control of the digestive tract.* I am especially interested in this subject because of its highly probable relationship to the etiology of "peptic" ulcer in man. I have had sufficient contact with "peptic" ulcer patients to realize *the rather important role played by sustained anxiety* and *the associated unhygienic eating habits* in the *genesis of ulcer.*

One of the most interesting developments in modern physiology has been the demonstration by Pavlov that, as a result of a learning or conditioning process, a *non-instinctive stimulus may excite or inhibit the gastric or salivary glands.*

The methods by which conditioned excitation and conditioned inhibition may be produced are illustrated in the following diagrams.

It is pertinent to my subsequent experiments and discussion to point out some of Pavlov's observations pertaining to the effect of the conflict of excitatory and inhibitory processes on the nervous system (1). A balance between the two is not easily attained and the dog frequently becomes quite restless. Occasionally such a conflict may result in a pathological state (neurosis), in which a predominance of one or the other process, depending on the temperament of the dog, is observed. In a "lively" dog the elaborated inhibitions may disappear and all stimuli provoke an excitatory response; in a "quiet" dog the opposite may occur.

I have attempted to ascertain if Pavlov's observations on the salivary glands might be applicable to the motility of the stomach. That is, I desired by appropriate conditioning to produce hypermotility or tonus of the gastric musculature. This attempt was predicated on the following fact: *The central nervous mechanism which is responsible for the psychic inhibition of the motility of the stomach may be conditioned.*

For example, the pain caused by the insertion of a hypodermic needle will cause not only a "defense reaction" but also will inhibit hunger contractions in the dog; but, after this is repeated a number of times, this pain no longer causes inhibition. However, if a new type of pain stimulus is applied, motility will be inhibited. In this instance, the dog has been conditioned to "ignore" the apprehension associated with the pain. The inhibition has been extinguished. After adequate training the dog can be subjected to a number of different types of mild pain stimuli, noises, etc., even new in type, without inhibition of motility of the stomach. The dog apparently no longer fears that he will be injured, regardless of the newness of the stimulus.

To so condition a dog, which has previously been trained to lie quietly, the head is patted, or the ear is tickled (pleasant to the dog), or the dog is spoken to, prior to and during the application of the needle prick or pain stimulus. After a brief period of training, it becomes unnecessary to "forewarn" the dog, except occasionally, since now the needle prick, or pain stimulus, may be applied without the dog manifesting a defense reaction or inhibition of motility.

Before proceeding with an interpretation of these phenomena, it is necessary to point out that

*From the Department of Physiology and Pharmacology, Northwestern University, Chicago, Illinois.
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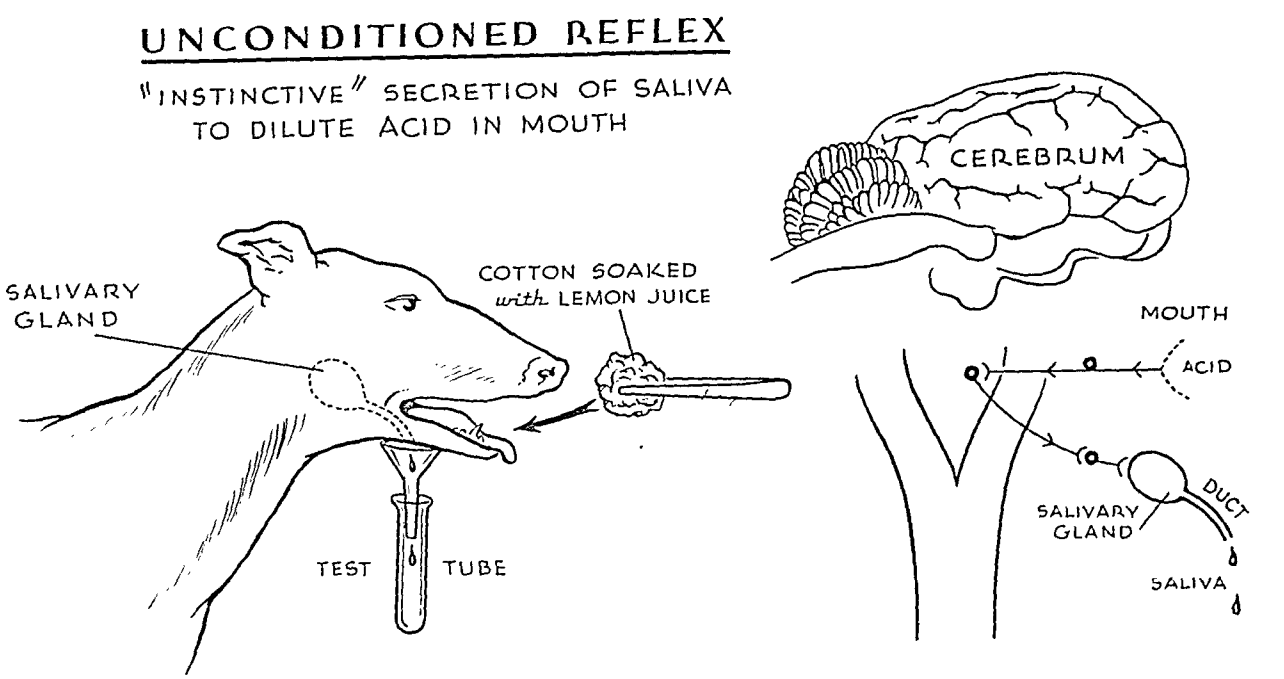


Fig. 1. The secretion of saliva in response to acid (lemon juice) applied to the mouth is an unconditional reflex, not involving the cerebrum.

in this experiment we are dealing with an "instinctive" or an *unconditional inhibitory reflex* (bulbo-spinal). This is in contradistinction to the salivary acid reflex that Pavlov deals with, which is an "instinctive", or an *unconditional excitatory reflex*. However, it is true that if a destructive or pain stimulus be associated with the giving of food, the defense reaction disappears and the pain stimulus may even become a *conditioned excitor* of salivary secretion (Ref. 1, page 186). The center for the defense reaction to pain is now inhibited and the salivary center is stimulated. Pavlov says, "the stimulation which entered into the center for defense reaction, now passes over to the food center", and, "that there is merely a transference, an alteration of direction, an attraction of energy from one center to another". In our experiment the patting of the head (pleasant stimulus) inhibited the defense reaction center and completely "blocked" or inhibited the splanchnic and vagal gastric inhibitory centers, (vide infra, psychic inhibition of motility is chiefly mediated by the splanchnics). But "energy" did not flow or irradiate into the vagal gastric motor excitatory center to cause hypermotility and tonus, i. e., *a reversal of the primary inhibitory effect did not result.*

I thought that by training the dogs (six) not to manifest inhibition of motility on pinching and pricking a number of areas (six) of the skin that I might obtain hypermotility and tonus. The result was that one could stimulate a large number of areas of the skin in succession, or two simultaneously in succession, or even "new" skin areas without obtaining any evidence of hypertonus. The dogs in so far as their skeletal musculature was concerned manifested either rigidity or a marked relaxation, but they did not fall asleep. This is possibly analogous to the *hypnotic state in animals* as described by Pavlov. In this connection it is well known to those who have studied gastric hunger motility in dogs, that some dogs react to the process of training them to lie quietly by manifesting muscular rigidity. These dogs are generally discarded because of the *irregularity of their contractions* and the variations in the tonus of their abdominal muscles.

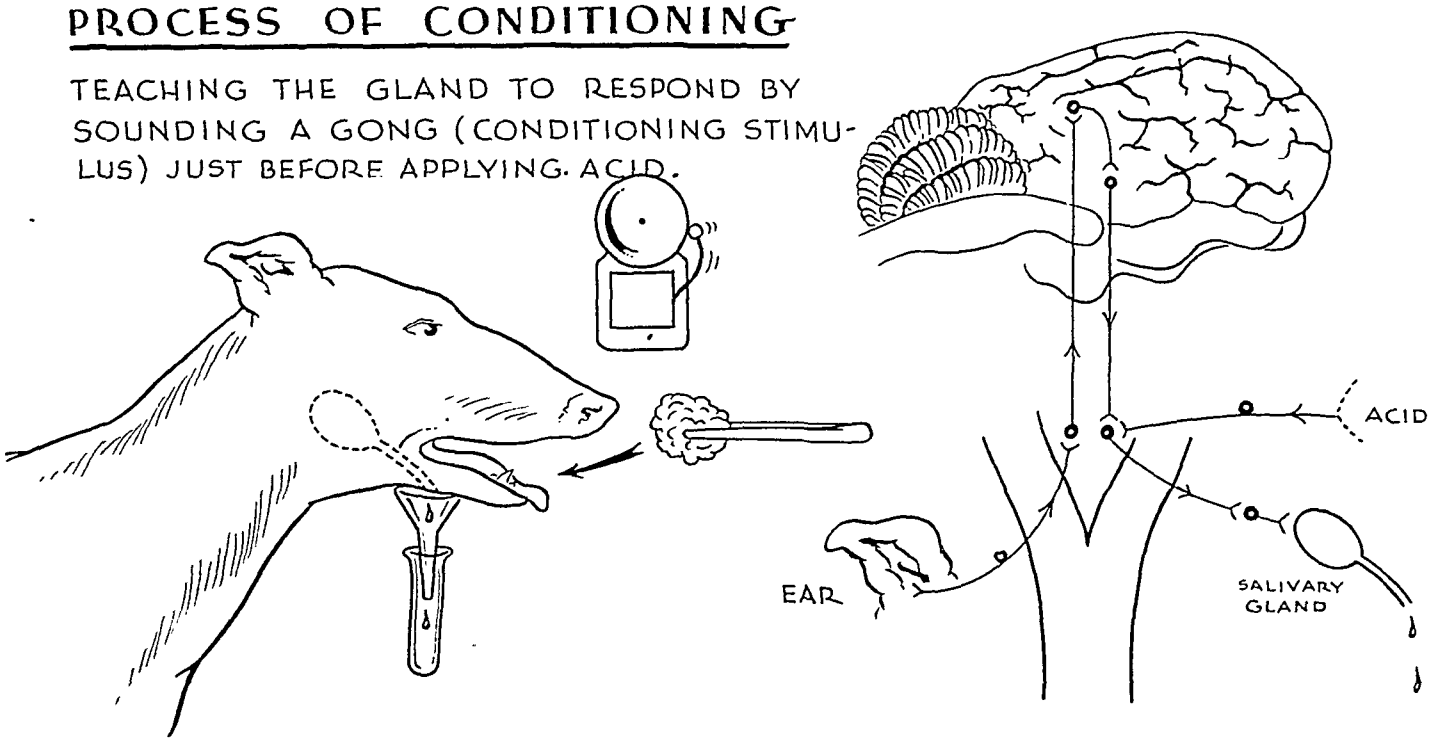
It would appear from the "failure" of my experiment that an inhibitory unconditional reflex by conditioning can be extinguished but cannot be reversed, and that this process of extinction is of such a nature as not to lead to the excitation of a closely correlated unconditional excitatory motor center (vagus center in this instance). It would also appear that the extinction by conditioning of an inhibitory reflex mechanism affecting an organ does not result in the release, due to withdrawal of inhibitory effect (in this instance chiefly the splanchnic), of the motor reflex mechanism affecting the organ (in this instance chiefly the vagus), although the irregularity of motility noted in some instances does indicate an *instability* of the central mechanisms. Further, it would appear that to obtain hypermotility and tonus of the stomach by a conditioning process it will be necessary to approach the stomach

through the vagal, or the predominant unconditional excitatory (motor) reflex mechanism. This will be very difficult, since the *only known approach of this kind* is via the vomiting center. Although the tonus of this center is augmented in hunger, this augmentation is probably not reflex in nature and hence cannot be used as an approach. In sleep the tonus of this center is also increased, but it is not clear how, by utilizing this mechanism, a hypermotility of the stomach during the waking condition could be produced experimentally by a conditioning process.

Several fundamental considerations arise from the foregoing experimental results and discussion, which to my knowledge have not yet been discussed in the literature on conditional reflexes. *The first is* that prior to the foregoing experiments no attempts have been made to modify by conditioning an unconditional inhibitory reflex mechanism. The studies have involved the elaboration of excitatory and inhibitory conditional reflexes of an excitatory unconditional reflex mechanism. That is, by sounding a gong, before and during the time acid (unconditional stimulus) is applied to the mouth, one can develop a positive or an excitatory conditional reflex; and by appropriate experimentation, one can develop a negative or inhibitory stimulus which will inhibit the conditioned excitatory influence of the gong. This is equivalent to saying that the excitatory effect on salivary secretion of a positive conditional stimulus may be prevented by a negative conditional stimulus. *The second* is that it has not been shown by a crucial experiment that a negative or inhibitory conditional stimulus (a conditioned inhibitor) when applied will inhibit or extinguish the acid salivary reflex, or an excitatory unconditional reflex. That such is possible one might presume from the above experimental results in which a bulbo-spinal inhibitory reflex was extinguished by conditioning. *The third* is that by conditioning one cannot convert an instinctive or unconditional excitatory mechanism into an inhibitory mechanism or vice versa (a secretory process does not lend itself well to such a study, but a motor process does). Theoretically, an excitatory or inhibitory response might occur as a release phenomenon (e. g., on blocking the inhibitory portion of a nervous mechanism, the excitatory portion may predominate and become more evident), but this did not result in my experiments.

Closely allied to the foregoing experiments and discussion is the old question of whether the autonomic motor control of the digestive tract has representation in the cerebral cortex. Fulton and his associates (2) have recently reported that stimulation of the pre-motor area of the cortex in monkeys and chimpanzees results in vigorous movements of the intestine. They believe that this provides an explanation for the morbid hunger and intussusceptions which sometimes develop after bilateral extirpation of the pre-motor areas. The facts, on the one hand, that sleep and decerebration (King, in guinea pigs) augment motility and, on the other hand, that dreams and

Fig. 2. The development of a conditioned reflex. The association of the sound of the gong just before and during the application of lemon juice opens up a new pathway involving the cerebral cortex.



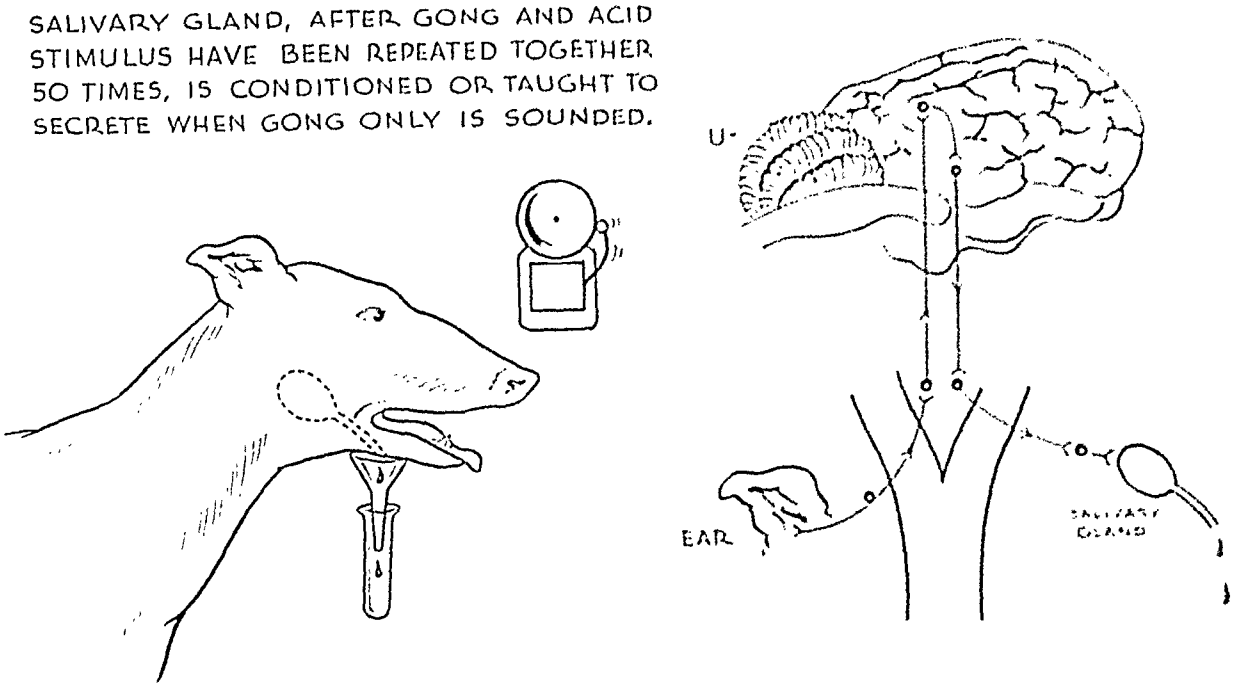


Fig. 3. The conditioned reflex has now been developed. The new pathways that have been opened up are adequate to excite a secretion of saliva when the gong only is sounded.

apprehension usually inhibit motility (3), indicate that the primary influence of the cerebral cortex on motility is inhibitory in nature. The exaggerated motility on stimulation may indicate a release of lower autonomic centers from cortical inhibitory control, rather than direct stimulation. In the experiments cited above we were unable to obtain such a release phenomenon. Nevertheless, I believe that the facts indicate that although cerebral activity generally results in an inhibition of gastro-intestinal activity, hypermotility and tonus of the stomach may be produced experimentally in the dog when the adequate conditions are ascertained.

What are the observed effects of anxiety and emotion on the motor activity of the stomach? The inhibitory effect of anxiety and anger was first directly observed in man by Beaumont. It was later studied in some detail in lower animals by Cannon (4) and Carlson (3).

As a general rule apprehension inhibits both the motility and secretion of the stomach. In lower animals no one, so far as I know, has seen any other effect. In man, radiologists (5) know that apprehension or mental shock causes the stomach to "drop" and become "flatter" in contour. I personally have seen the stomach of students drop in response to a threat and rise again and resume motility on provoking laughter by passing the threat off as a joke. Gastric emptying is definitely delayed by quizzing a poorly prepared student. It is not usually delayed by quizzing a good student who has faith and confidence in his ability to answer questions correctly. However, I am quite certain that occasionally strong emotion may cause spasm and hypermotility of the stomach without nausea and vomiting being experienced. The literature, in so far as actual evidence is concerned, is silent. Alvarez (6) has told me of two patients suffering from pain in the epigastrium following strong emotional stress in whom he made X-ray studies. In both instances he observed five or six deep waves passing over the stomach simultaneously, the stomach presenting the appearance of a sock filled with billiard balls. I have seen a similar picture in a hysterical young woman, in which detailed examination and other considerations revealed that the disturbance was not due to a viscero-visceral reflex or organic disease. Thus, it would appear that apprehension as a general rule leads to an inhibition of motility, but may in some subjects result in marked hypermotility and tonus of the stomach.

Todd (7) has made the most intensive study to date of the effect of anxiety on the human stomach. His subjects were medical students. He started his studies during the early apprehensive weeks of the "new life" of a modern medical student and continued with the same students for several years. He has reported that the "stable stomach" does not respond readily to emotional factors and is found in persons with an "even temperament". Many of his first-year students

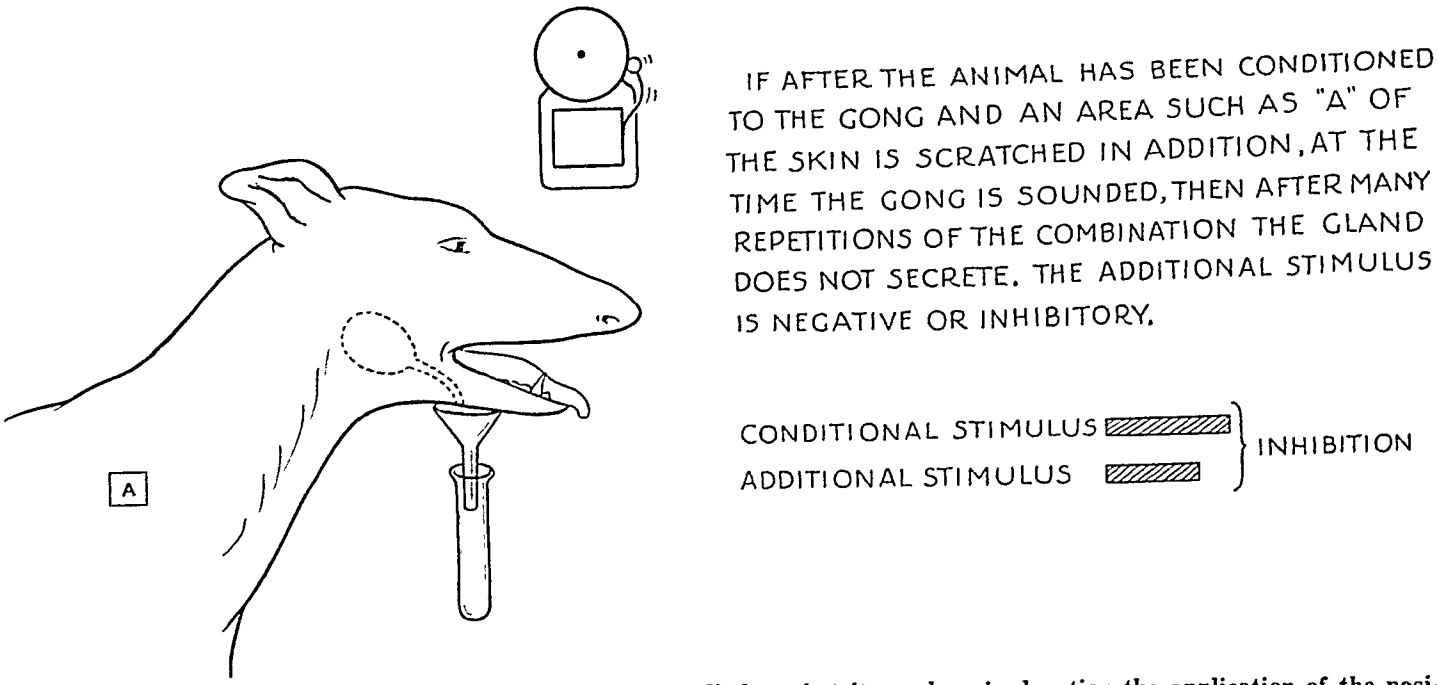


Fig. 4. When an "additional", or a second, stimulus is applied so that it overlaps in duration the application of the positive conditional stimulus (the gong), and the combination is repeated many times without the application of lemon juice, or the unconditional stimulus, then the additional stimulus becomes a "conditional inhibitor".

manifested an "unstable stomach" in that "dropping" and inhibition of movements of the stomach occurred on subjecting them to emotional factors. The stomachs of his second-year students were more stable. Thus, as shown in the "pain" experiments on the dog cited above, through training or conditioning, the stomach may no longer be affected by inhibitory psychic factors. A more significant observation, however, was made, namely, that when the "conditioned or trained" stomach shows instability in response to more prolonged mental distress, the instability takes the form of hypermotility. Todd has stated "hyperactivity of the stomach is always present in the anxiety complex and in patients consciously or subconsciously nervous but not afraid".

Over what nerves are the above effects transmitted to the stomach? Before this question can be clearly answered it is necessary to consider briefly the functional innervation of the stomach. Much of the recent work on this subject is confusing to the average reader. This is because of the actual complexity of the functional innervation of the stomach. For example, both motor and inhibitory effects may be obtained via either the splanchnics or vagi (8). However, one must not permit details, although important, to fog a true conception of the predominant functional innervation of these nerves.

By sectioning the splanchnic nerves in dogs, it has been shown that psychic inhibition of gastric motility is almost entirely abolished (3). This leads us to believe that the splanchnic nerves are primarily concerned in the psychic inhibition of gastric motility and tone.

But, the mechanism concerned in the production of the augmented motility that Todd reports as occurring in the unstable, conditioned stomach in the presence of sustained anxiety is not so clear. This is because such a condition has never been produced in lower animals in which the nerves may be experimentally sectioned. The vagi very probably are primarily concerned, because of the following considerations. They are the predominant motor nerves of the stomach. Following the section of the vagi in animals a permanent hypotonus and delay in evacuation of pastes and solids results (9), though liquids may soon be evacuated in normal time. Following section of the splanchnic nerves in man colic may occur which is relieved by atropine (10).

In spite of Crile's (11) interesting theories it is difficult to believe that this hypermotility and tonus are induced chiefly by the splanchnic nerves. However, it is true that spasm of the pyloric sphincter may be induced reflexly via the splanchnic nerves and that epinephrine in adequate dosage causes the sphincter to contract (12). It is possible that given a contracted sphincter the stomach will manifest compensatory vagal hypermotility. But, epinephrine inhibits gastric motility. (No one has studied the effect of psychic factors on the pyloric sphincter.) It is also pertinent that stimulation of the splanchnic causes vaso-constriction of the gastric vessels. This means that in anxiety some constriction of the gastric vessels may occur and cause some asphyxial spasm of the gastric musculature; but this could not continue for any length of time in the fundus of the stomach in view of the continuance of the normal or hypernormal secretion of the

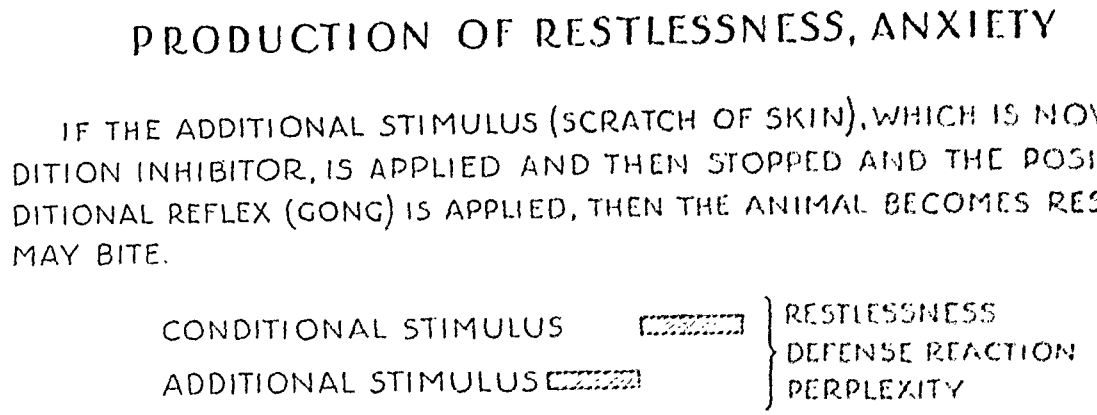


Fig. 5. When an inhibitory conditional stimulus reaches the cerebrum and then is immediately, or quite soon, followed by an excitatory conditional stimulus, a conflict occurs. Restlessness, or anxiety (subjective, of course) is the result.

hypermotile stomach. It is difficult to picture how the peristalsis in the pyloric antrum could continue, since a mild degree of anoxemia inhibits motility, although it does induce spasm of the sphincter (13). Of course, it may be argued, in so far as the etiology of "peptic" ulcer is concerned that the hypermotility of sustained anxiety is due chiefly to the vagus and that this is associated with an increased splanchnic vaso-constrictor tone of the vessels of the mucosa. Because of the foregoing type of speculation required in any attempt to rationalize the procedure of adrenal denervation for "peptic" ulcer, it is difficult for a physiologist to warm up to the idea.

However, I have yet to meet a clinician of extensive experience who denies that sustained anxiety is a factor in determining the chronicity and recurrence of "peptic" ulcer in many cases. In this connection, Todd (7) reports that students may have hyperactive tracts for several years without developing ulcer, but hyperactivity was evident in those of his students who later developed the symptoms of ulcer.

We (14) have recently attempted to determine in the dog whether the maintenance of continuous hypermotility and hypersecretion of the stomach for a period of two months will result in chronic ulcer. One group of animals was injected every two hours with pilocarpine, a second group with histamine, and a third group with both pilocarpine and histamine. Acute lesions of the stomach and duodenum were observed, but no chronic or perforating ulcers were produced.

It would appear from these studies in the dog that some other factor besides hypermotility and secretion is necessary for the production of a chronic "peptic" ulcer. It should be remarked that these animals were fed a "smooth" diet, and the results might have been different on a "rough" diet. These drugs, of course, would probably not exert a direct "neurotrophic" effect or a vaso-constrictor action, which are the only other factors which have been suggested as being concerned in the "anxiety-ulcer" relationship. That a "rough" diet and hypermotility and secretion are factors conducive to ulcer are generally recognized and have much experimental support.

The major facts pertaining to the functional innervation of the pyloric sphincter may be briefly summarized as follows: the sphincter usually contracts on noxious stimulation of the gall bladder, colon and appendix (12), (15), (16). The motor side of this reflex is primarily in the splanchnics. At the same time the stomach is inhibited unless nausea and vomiting occur in which instance the antrum contracts via the vagi. The vagi are concerned in the inhibition of both the sphincter and stomach when the duodenum is mildly stimulated (enterogastric reflex) (17). This mechanism normally retards gastric evacuation. In the instance of irritation of the duodenum, the local Meissner-Auerbach's plexus is concerned in causing contraction of the sphincter without inhibition of gastric motility (17). This mechanism may be concerned in the delayed evacuation with hypermotility in cases of duodenal ulcer. Cases of duodenal ulcer that empty more rapidly than normal are to be explained by the more rapid rate of emptying of the duodenum, associated with the hypermotility of the stomach.

Reflex pylorospasm and vomiting occur in dogs with splanchnics sectioned.

In regard to the autonomic innervation of the *biliary tract*, I shall only point out that atropine favors the flow of bile from the common duct and pilocarpine has the opposite action. Atropine decreases the tone of the gall bladder but does not prevent the action of cholecystokinin. Pilocarpine causes some contraction of the gall bladder, but no bile is expelled into the intestine because of the simultaneous increase in the choledocho-duodenal resistance (18).

Passing on to the *intestine* there is a point pertaining to appetite and intestinal obstruction which demonstrates a significant function of the automatic innervation of the gastro-intestinal

tract. In a study of continuous jejunal alimentation in two dogs, we observed that as long as we kept the intestine filled with food the dogs showed no desire to eat in the normal manner. However, after sectioning the vagi these animals manifested an inordinate appetite even to the extent of coprophagia. This shows that the feeling of satiety depends to a large extent on the vagus and that distension or irrigation of the intestine, like the stomach decreases appetite. This was shown more strikingly by Herrin and Meek (19). They continuously distended an isolated loop of intestine. A very copious secretion of intestinal fluid resulted, the dog would not eat and drink, became dehydrated, developed hypochloremia and died. However, after the nerves of the loop were sectioned, the dog would eat and drink, and survived in spite of the continuous loss of fluids and chlorides. This demonstrated that the prime factor in the serious consequences of simple obstruction without strangulation is the loss of water and chlorides.

A consideration of the motor innervation of the *ileo-cecal sphincter* is of practical importance in that it may explain ileo-cecal intussusception that sometimes occurs in infants and after appendectomy in adults. The sympathetic supply of the ileo-cecal sphincter is definitely motor in its function. The vagi have both a motor and inhibitory effect on the sphincter, which, however, is slight when compared with the motor effect of the sympathetic (20). If, during or following appendectomy the sympathetic supply to the sphincter and lower ileum is sectioned or affected, the sphincter will become patulous and the lower ileum hypermotile. This would increase the likelihood of the ileum undergoing intussusception into the cecum. Ileo-cecal intussusception is the most common type in the infant. According to Zamorani (21) the coeliac ganglion does not mature histologically until about two years of age. If this is true physiologically, we have the explanation for the clinically observed vagotonic tendency of the infant's gastro-intestinal tract. In addition the infant would have an atonic ileo-cecal sphincter which with a hypermotile ileum would predispose to ileo-cecal intussusception.

Our knowledge of the functional innervation of the *colon* of man is rather sketchy. We know much more concerning this subject in lower animals (22). Because of the rather marked anatomic differences some physiologists have hesitated to apply their work to man. However, this reticence is not entirely justified as has been demonstrated by the recent surgical treatment of Hirschsprung's disease. For years physiologists have known that the predominant parasympathetic effect was excitatory for the colon musculature and inhibitory for the sphincters, and that the predominant sympathetic effect was inhibitory for the colon and excitatory for the sphincters. It now appears to be established that section of the sympathetic supply of the colon in Hirschsprung's disease markedly alleviates the obstipation. The obvious result is relaxation of the smooth muscle sphincters of the colon and an increase in the propulsive activity of the colon.

Physiologically I believe the irritable or "unstable" colon is quite analagous to the "unstable" stomach which was discussed above. Clinically it is recognized that many "peptic" ulcer patients have an "unstable" colon. In both conditions belladonna, bland diet and sedation are used therapeutically. In regard to the "unstable" colon and cecal stasis a physiologic fact that is not fully appreciated is that the colon throughout its course manifests the phenomenon of receptive relaxation. This is true for the rectum as is well known. It is particularly true for the cecum. It is also true of the transverse and descending colon. The application of this fact, I believe, is obvious.

In certain abnormal conditions of the colon large quantities of mucus are produced. The evidence indicates that this is not due to a direct stimulation of secretion by nerves. However, prolonged stimulation of the pelvic nerves, repeated injection of pilocarpine, or the introduction of irritants into the colon increases the production of mucus. This would indicate that the augmented secretion is chiefly due to irritation of the mucosa and excessive motility. Extracts of the colon mucosa according to Florey (23) do not increase mucus production.

It is of clinical interest that fear or apprehension causes pallor of the mucosa of the colon, even in the absence of the adrenals (24). If an area is inflamed, pallor does not result. This pallor is due both to a general contraction of the vessels of the mucosa and to a squeezing out of blood by contraction of the muscularis mucosae. The colon, on mechanical stimulation, shows a patchy pallor due to irregular contraction of the muscularis mucosae.

I next desire to discuss briefly some of the more important *viscero-visceral reflexes.* I shall not mention the exceedingly important, and very interesting and instructive, viscero-skeletal or viscero-somatic reflexes.

It has been well demonstrated that the sympathetics conduct sensory sensations responsible for the elicitation of visceral pain, muscular rigidity, cutaneous hyperesthesia and vaso-motor disturbances (25), (26). The vagi conduct sensations which elicit nausea and vomiting, affect appetite, and which is the case of the stomach mediate impulses that are responsible for satiety. The sensory pathway for crude heat and cold sensations for the stomach is not known. These nerves also mediate sensory impulses concerned in viscero-visceral reflexes. The pelvic nerves are mixed in regard to their sensory activity.

Gastro-ileo-colic and Duodeno-ileo-colic Reflexes: When food is ingested a reflex is initiated from the stomach and especially from the duodenum which causes rather rapid evacuation of

the distal ileum into the colon. This, in all probability, increases the activity of the colon. This, in turn, accounts for the early *post cibum* distress of the patient afflicted with colitis.

The importance of this reflex did not impress me until several years ago when we (20) made a study of the ileo-cecal sphincter. We observed that when some barium milk was placed into the distal ileum of a fasting dog through an ileostomy, it was retained there for one-half hour or longer. After the ingestion of food, the barium milk was evacuated into the cecum within fifteen minutes. The nervous mechanism of this reflex has not been determined.

Cholecysto-gastric Reflexes: Recently Fishback and I studied (27), (3), (16) the effect of biliary tract distension and irritation on the movements of the stomach. We observed that mild stimulations inhibited gastric motility and decreased tone. This type of response, according to my views, is conducive to gastric flatulence and air swallowing (28). A sudden marked distension caused pylorospasm with nausea and vomiting. This accounts for the dyspeptic symptoms of gall bladder disease. But, the pain of biliary colic is not due to pylorospasm because the type of referred pain is different and biliary tract pain may be obtained in man and dog following subtotal gastrectomy (18).

Appendico-gastric Reflex: The fact that the diseased appendix may reflexly affect the stomach is indirectly one of the reasons why the mortality of appendicitis is still so high in this country. The lay person thinks the symptoms are due to a "stomach upset" and takes a physic or enema, which results in rupture and peritonitis. The physician, if called early, can save the life of practically every patient with appendicitis.

Experimentally distension of the appendix and cecum in the dog results in inhibition of the gastric movements chiefly via the splanchnic nerves (8), (14). The pyloric sphincter generally contracts—an effect that is mediated chiefly via the splanchnics also. (Inhibition of the sphincter may also result) (3), (12), (15). Marked distension of the appendix and cecum, particularly if the latter is irritated, causes pylorospasm and frequently vomiting. Under such conditions it is difficult to determine whether the dog suffers epigastric pain or not. Dr. Livingston of New York has written me that when the appendix in man is distended, epigastric pain, nausea and sometimes vomiting, result. Right lower quadrant pain, point tenderness, and cutaneous hyperalgesia followed immediately. In this connection, Loreti (29) has reported that after anesthetization of the right lower quadrant the pain in that segment disappears, but the epigastric pain persists.

Of course, epigastric pain does not always occur in appendicitis. Neither can the same type of viscero-visceral reflex always be elicited with the same stimulus in dogs. This must mean that either the reflex threshold is very high or other factors inhibit the reflex.

Smith and Miller (16) have found in patients that distension of a spastic colon may produce gastric spasm with severe epigastric pain, which is not elicited after atropine. This again indicates, as referred to above, that spasm of the pyloric antrum in contradistinction to the pyloric sphincter is due chiefly to the influence of the vagus.

It should also be borne in mind that irritation of the colon, cecum and appendix reflexly causes the ileo-cecal sphincter to contract. This has been demonstrated in animals (20) and ileal stasis has been observed in man by Hunt, Cole and Kantor (30).

Reflexes Between the Genito-urinary and Gastro-intestinal Tracts: Reflex changes in the stomach analogous to those described above may be elicited by stimulation of the genito-urinary organs (3), (31). This should be borne in mind because patients have been treated for "dyspeptic" symptoms when the real source of their trouble was resident in the urinary tract.

Time does not permit me to proceed further. Such rather interesting and important gastro-intestinal viscero-visceral reflexes or effects as the colon-duodenal, viscero-cardiac (32), (33), (34), and reflexes within the colon itself (35) may be mentioned in passing.

Often when I contemplate the many mechanisms in the gastro-intestinal tract which may get out of order, and the fact that mental activity may throw some of them out of order, I think of the statement of Josh Billings, to wit, "I have finally kum tu the konklusion that a good reliable sett of bowels is worth more tu a man than enny quantity of brains".

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The Effect of Mechanical Stimulation of the Duodenum, Colon and the Stomach on the Cerebral Circulation and Intracranial Pressure*

By

JOHN VANDOLAH, M.S.

and

LATHAN A. CRANDALL, JR., M.D., Ph.D.

CHICAGO, ILLINOIS

GASTRO-INTESTINAL disturbances appear to be an important element in many cases of headache, including some which present the typical features of migraine. Individuals in whom headache follows the ingestion of certain foods, or is secondary to constipation or other disturbance of function in the alimentary tract, frequently are met with. There is at present no evidence to show whether in these instances headache results from the absorption of toxins of an undetermined nature, or whether a reflex mechanism is concerned.

The purpose of the present study was to investigate the possible existence of a reflex mechanism. That is, to determine whether mechanical stimuli applied to the viscera would give rise to sensory impulses which, acting through centers in the brain and cord, might bring about changes in the tonus of the cerebral blood vessels with secondary effects upon intracranial pressure.

A number of previous investigations by others have suggested that alterations in pressure and flow in the vessels of the brain may be concerned in the production of headache. An anatomical basis for this hypothesis has been supplied by Stöhr (1) and Hassin (2) who demonstrated that a perivascular plexus surrounds the arteries of the cerebrum. It is well known that the nitrites may produce headache in human beings; Leake (3) and his co-workers have shown that the cerebral and the retinal vessels dilate when drugs of this group are administered. Chambers (4) has reported constriction of the retinal vessels in the prodromal stage of an attack of migraine.

*From the Department of Physiology and Pharmacology, Northwestern University, Chicago, Illinois. This work was aided by a grant from the Josiah Macy, Jr., Foundation.
Submitted November 24, 1934.

METHODS AND MATERIALS

We have measured changes in the size of the meningeal and retinal vessels while stimulating the stomach, duodenum and colon by distension with a balloon.

1—A series of ten cats and seven dogs lightly anesthetised with Nembutal was studied, using the technique described by Forbes (5). A trephine orifice was made in the parietal bone, the dura mater was incised, and a glass window was inserted into the opening. A microscope fitted with a micrometer ocular was employed in order to make direct observations of the pial vessels. Illumination was secured by a small lamp which focused the light obliquely down upon the field. A balloon attached to a rubber tube then was placed in the duodenum through an incision near the pyloric end of the stomach and held there by a purse string suture. The diameter of a vessel was measured several times before mechanical distension of the duodenum by means of the expansile balloon. The balloon was inflated and measurements again taken. The calibre of the vessels was noted once more after deflation of the balloon. The like procedures were followed with the balloon placed in the stomach and in the colon. *No change in the calibre of the pial vessels could be observed when a balloon in the duodenum, the stomach or the colon was distended.*

2—It has been pointed out by many observers

that alterations in the size of the cerebral and renal arteries occur simultaneously. By taking advantage of this established fact, we were able indirectly to measure the cerebral vessels during visceral stimulation by observing the retina.

Four human subjects swallowed Rehfuss tubes to which small balloons were attached. The tubes entered the duodenum in two cases (checked by X-ray) while in the other two they remained in the stomach. Through the co-operation of Dr. W. A. Mann, Jr., of the Department of Ophthalmology at Northwestern University Medical School, pictures of the fundus were taken with the Zeiss-Nordesen fundus camera before, during and after distension of the stomach or the duodenum. In two patients, nausea was experienced, and it was accompanied by retching in one of the subjects. In the two other patients, vague epigastric sensations and dizziness were noted. Measurement of the retinal vessels in the fundus photographs revealed no change in their sizes when a balloon in the stomach or in the duodenum was distended.

3—In the animal experiments we had observed that during distension of the viscera, the cerebrospinal fluid appeared to be increased in volume. It is well known that changes in general circulation, particularly in venous flow, influence intracranial pressure. If it could be shown that intracranial pressure varied without corresponding changes in the general, vascular pressure when the viscera were distended, it might be assumed that the intracranial pressure changes were due to alterations in the sizes of the cerebral vessels.

In order to test this possibility, ten lightly-anesthetised dogs were used. A trephine opening was made in the parietal bone, a crucial incision was made in the dura, the flaps were pulled back over the edges of the bone and a hollow metal plug was screwed into the opening (a modification of Eyster's apparatus (6). This plug was connected to a tambour by a rigid-walled rubber tube which was filled with warm Ringer's solution. Simultaneous tracings then were secured of intracranial pressure, the arterial pressure from the carotid artery and the venous pressure from the right atrium. As a next step in the procedure, a balloon was placed in the stomach, the colon or the duodenum in accordance with the technique described above. *In all instances during distension of the balloon, venous and intracranial pressure rose.* The arterial pressure rose in some cases, fell in others, but on two occasions it did not change. When the balloons were deflated within a short time all pressures returned to normal.

The rise in intracranial pressure on distension of the viscera, in all probability, is secondary to the venous pressure increase; it is not due evidently, to changes in the caliber of the cerebral vessels. The increase in venous pressure amounted to 3.0—12.0 cm. H_2O. One should consider the possibility that such venous pressure-changes, accompanied as they are by increases in intracranial pressure, might be adequate stimuli to pain fibers in the cerebral perivascular plexus. In this connection one is tempted to recall how commonly there is experienced relief of dull, cephalgic discomfort after a complete evacuation of the bowel.

CONCLUSIONS

1. No measurable changes in the calibers of the cerebral vessels could be demonstrated when the duodenum, the stomach or the colon of cats or dogs was distended.

2. No measurable changes in the caliber of the retinal vessels of humans could be demonstrated when the stomach or the duodenum was distended.

3. An increase in intracranial pressure on distension of the hollow viscera was observed only when there was a concomitant rise in the venous pressure.

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ABSTRACTS

McMASTER, PHILIP D., AND DRURY, D. R.

Irreversible Character of the Late Changes After Hepatectomy. J. Exper. Med., 60:503-513, October, 1934.

A series of experiments were done on hepatectomized rabbits. Continuous cross-transfusions were effected between normal and "liverless" rabbits to determine what changes, if any, occur. These experiments show clearly that such cross-transfusions failed to improve the advance symptoms due to previous hepatectomy. In addition, the normal rabbit failed to show any deleterious effect from the blood of the hepatectomized animal.

The authors conclude that the symptoms of advanced liver insufficiency are irreversible and cannot be explained alone on the basis of the accumulation of toxic substances within the blood.

The clinical significance of this experimental work is certainly unfavorable towards the administration of any "biological" preparation to patients suffering from advanced liver insufficiency.

M. G. Vorhaus, New York, New York.

Growth of Diabetic Children

By

HENRY J. JOHN, M.D.
CLEVELAND, OHIO

IT HAS been emphasized in the literature that diabetic children are tall in stature. White[1] in her studies states that "stature in excess of standards in common use today is the rule. This excess amounted to an average of 2.2 inches above the Crum & Wood standard in 227 children . . . and the excess occurred in 86 per cent of the cases". Ladd[2] reported overgrowth in 88 per cent of his juvenile diabetics and Rabinowitch-Bazin[3] in Montreal found it in 71 per cent. Boyd and Nelson[4] also report overheight in 75 per cent of their cases. Puchulu[5] reports 50 per cent of his cases as overheight and the other 50 per cent were below the height for their age. Spencer[7] in a study of 45 diabetic children points out particularly the fact that, at the onset of the disease, 80 per cent of his patients were normal height or above for their ages; 57 per cent were at least one inch above normal height for their ages. He

Submitted December 5, 1934.

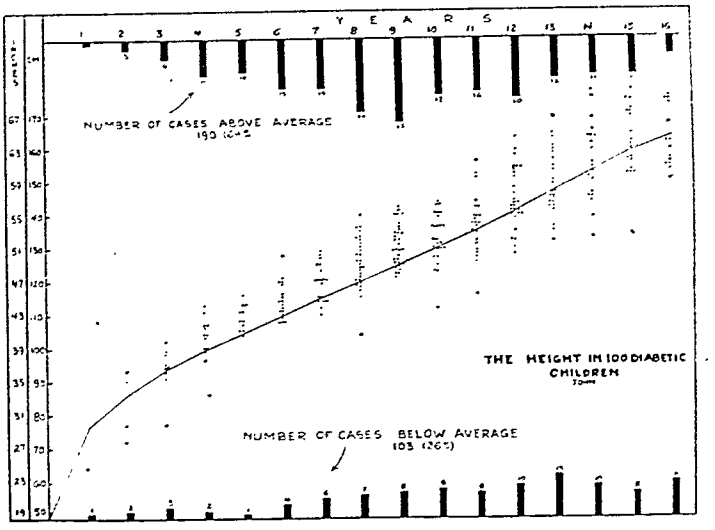
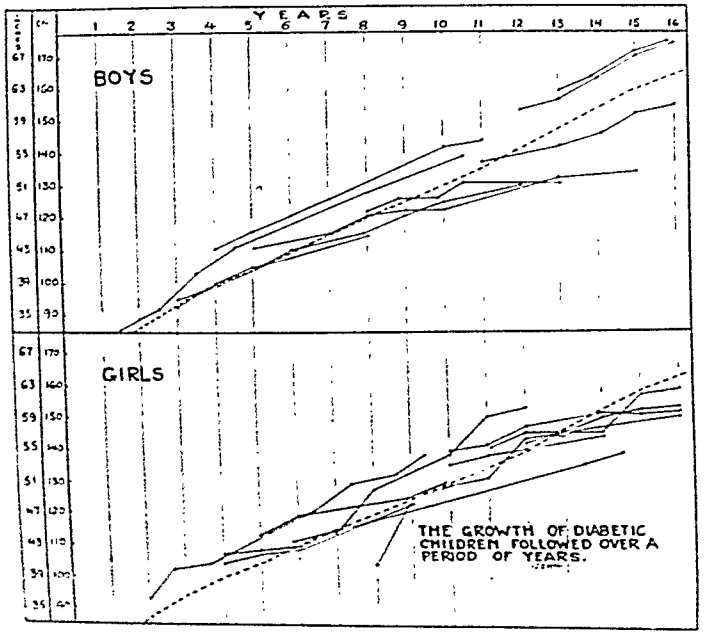


Chart 2. Data on the measurements of height of diabetic children at the various age periods as compared with normal standards. 293 measurements showing the number above and below the normal curve.

Chart 1. The growth of diabetic children, boys and girls, followed over a period of years. Each connected graph represents one child.



states: "The typical diabetic child at the time of onset of the symptoms of the disease is tall and slender (overheight for age and underweight for both age and height)". However, he points out that as the child progresses in this disease, there is a decrease in the rate of growth. This, of course, is all the more striking since it has been shown that, prior to developing the disease, these children had grown in height more than had the average child.

Rabinowitch and Bazin[3] make the statement that "whatever the stimulus is that causes diabetes in children, it is also responsible for the excess of skeletal growth. That in view of the present knowledge of the relationship between skeletal growth and the anterior lobe of the pituitary gland and the alleged association between that part of the gland with the sympathetic nervous system, the question arises: is diabetes, occurring in children who are overheight, of pituitary origin?"

In an editorial of the *Journal of the American Medical Association*[10] the suggestion is made that diabetes may not be a disease of the pancreas

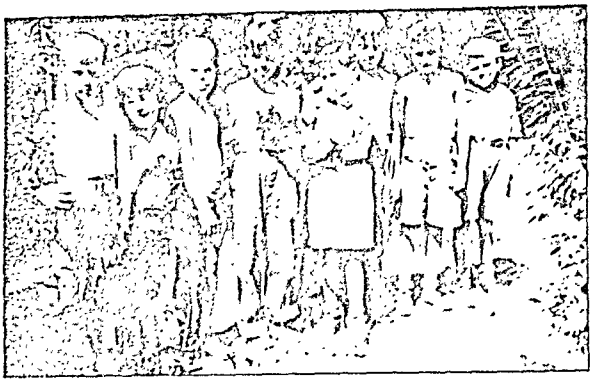


Fig. 3. A group of diabetic boys 9 years of age.

alone but also may involve some of the other glands of internal secretion and consequently affect the growth and the development of children even before definite manifestations of a disturbed carbohydrate metabolism become evident. Whether this lack of growth, later on in the disease, is a characteristic of the diabetic disturbance rather than a defect in its management remains to be learned.

In Table 1, I have summarized the reports of growths in diabetic children as given in the literature. The predominance of increase in height is quite obvious.

In an attempt to analyze the gain in height in diabetic children, I have gathered data on 100 diabetic children out of my own series of 240. Most of these children have been followed over a period of many years. In general we can say that, at the time when diabetes first develops, the child, almost without exception, is above the normal average in his height, a fact mentioned by most authors. As time goes on, many of these children maintain the high normal average; others, after a period of few years, fall below the normal standard and from the thirteenth to the sixteenth year, several of the group fall into a group we might call "dwarfism". When we study Chart 1, in which data of height are given of the individual diabetic children followed over a period of years, the boys seem to predominate in this dwarfism over the girls. Again, from the fourteenth to the sixteenth year, the girls seem to drop considerably more below the normal standards. Nearly all start with statures at or above the normal when their diabetes first develops, but as time goes on. some maintain this growth while others fall below.

In Chart 2, I have given the summary of all the data, the measurements of height at the different ages of the 100 children with diabetes so as to get an idea of the picture as a whole. It is quite evident that the overgrowth predominates and the relationship of over- to under-growth is as 190:103, that is nearly twice as much. When, however, we take into consideration that, at the beginning of the disease, nearly all the children are above the normal average and only later many fall below, this ratio would be somewhat altered.

Fig. 4 represents a group of five diabetic girls of the same age, 12 years old. One can note the considerable contrast in the heights. The second from the left obviously is a dwarf in stature, whereas the one on the extreme right, much overheight and overweight for her age, is a case of endocrine disturbance.

This entire picture of the diabetic child today is quite different from what it was in the preinsulin era when we had to undernourish the diabetic child in order to keep him alive. With such an undernourishment, naturally we dealt with stunted growth. Such a picture most medical men had in mind up until some ten years ago, namely, that the diabetic child did not grow up to normal standards. Even as late as 1925, Joslin[9] wrote: "The increase in height of the diabetic child treated with insulin, though occasionally normal, is usually below that of the normal child. So far he has not grown tall like the normal child, either at the expense of growing thin, or while being well nourished."

TABLE I

The Incidence of Height in Diabetic Children as Given by Various Authors

Author	Number of cases	Above normal height per cent	Below normal height per cent
Boyd and Nelson[4]	32	75	
Geyelin		0	
John (present publication)	100	65	35
Ladd[2]	34	88	
Priesel-Wagner[3]	38	0	
Puchulu[5]	30	50	50
Rabinowitch, Bazin[3]	71	71	
Sherrill[6]	62	+	
Spencer[7]	45	80	
White[8]	227	86	

In cases where we deal with decreased growth, it remains to be learned whether this factor is characteristic of the diabetic disturbance rather than a defect in the management of the diabetes. The use of growth hormones is in its infancy and at present one feels reluctant to exhibit such preparations as a routine measure for those who

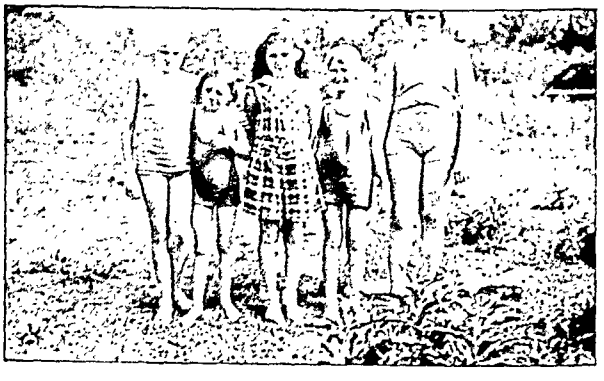


Fig. 4. A group of diabetic girls 12 years of age.

are undergrowth inasmuch as we do not know their ultimate effect on the other organs of internal secretion.

SUMMARY

1. Most authors agree that, at the onset of diabetes in children, the great majority of these are at or above the normal standards of height. As the disease progresses, many of these children seem to fall below the normal standards.

2. An analysis of 100 diabetic children from my own series, children who have been followed up over a period of years, almost without exception, the above statement holds. As time goes on, many of these children maintain this high normal level; others, after a period of few years, fall below the normal standard. This drop in height is most marked in the age period between the thirteenth and the sixteenth years. Few fall definitely into a group we might call "dwarfism". There were more of these dwarfs in my own series among the boys than among the girls.

3. This relationship of over- and undergrowth, in my series of 100 children, taken at large and over a period of years, showed nearly twice as many children above the normal standards.

4. Future studies will disclose whether this stunting in the growth in the later stages of diabetes in some children successfully can be combated by the use of extracts of the endocrine glands or whether a proper metabolic balance can be attained by proper nutrition and proper control of the diabetic condition alone.

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The Nutritional and Digestive System Aspects of Pernicious Anemia

(Part I)

By

L. G. ZERFAS, B.S., M.D., F.A.C.P.
INDIANAPOLIS, INDIANA

and

BEAUMONT S. CORNELL, M.D., F.A.C.P.
FORT WAYNE, INDIANA

DURING 113 years since the recognition of pernicious anemia as an entity, countless etiological hypotheses have been offered. Although today a more inclusive viewpoint is possible than at any previous time, the cause of the disease is not yet completely demonstrated. The newer knowledge of gastric physiology is the particular phase upon which hangs the best hope of an explanation for the involved pathogenesis.

If the spinal cord changes could be as readily co-ordinated with the gastric state as can the blood changes, the problem of the cause would seem to be nearing a solution. But it is well known that the degenerative changes in the nervous system may, at times, become actively progressive while the blood system is under satisfactory control by specific treatment. For this reason it is difficult to assume that the hemopoietic system and the nervous system owe to any common cause their dissociated manifestations.

A large proportion of the total knowledge of the disease relates to the digestive system. It has received almost as much clinical and pathological attention as has the hemopoietic system and more than the nervous system. If without reference to the literature a physician were to study the patients intensively he would be so impressed by the gastro-intestinal symptoms as to impute to them a causative role. This has been the history of the disease, for the profession has not been able to dismiss this strong intuitive attitude.

A common weakness in all etiological deliberation is to overemphasize a positive finding, even when it fails to explain the total manifestations of the disease. Again, a partially successful method of treatment, while invaluable from a practical and humanitarian standpoint, is seldom of equal value in pathological argument. While insulin gives a more striking control over carbohydrate metabolism than any known agent, it does not necessarily follow that diabetes mellitus primarily is a disease of the pancreas. Similarly, although the "x" substance found in liver,

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stomach, or produced by the action of the intrinsic factor of the stomach on protein, exerts a remarkable control over the blood-forming organs, it does not of necessity follow that the absence of this intrinsic factor is the sole and sufficient cause of the disease. It must be remembered, for example, that constitutional peculiarities are unusually marked in persons acquiring pernicious anemia, so that perhaps idiosyncrasies of bone marrow and of the nervous tissues are just as essential as are delinquencies of gastric secretion. This point might be settled by finding persons without the intrinsic factor who do not develop pernicious anemia.

It is not the purpose of this monograph to claim complete etiological significance for abnormalities found in the gastro-intestinal system, although it is the conviction of the Authors that no better lead exists. It is intended rather to show what a very large amount of the total investigation of the disease has centered around the digestive tract.

EARLY INVESTIGATIONS

In 1821, Combe of Edinburg, in describing pernicious anemia for the first time, felt instinctively that a nutritional problem was involved, since he wrote: "It is probably owing to some disorder of the digestive and assimilative organs that its characteristic symptoms have their origin." Elliotson's *Practice of Medicine*, 1846, refers to certain cases of severe anemia which were, no doubt, Addisonian, and he mentions the "bad appetite" and calls special attention to a group of cases in which the digestive symptoms dominated the clinical picture—dark, fetid stools, nausea and constant vomiting.

While Addison's famous communication of 1895, *On the Constitutional and Local Effects of Disease of the Suprarenal Capsules*, placed the disease forever on a firm basis as a generic entity, it rather slighted the digestive system, though he did not neglect to mention the failure of the appetite.

As early as 1851, the discerning Barclay (1) described for the first time the glossitis, which Hunter later developed into an important diagnostic sign.

Austin Flint, in 1860, and Fenwick, in 1865, emphasized certain degenerative changes in the gastric mucosa as possibly related to the cause of the disease. This, and similar conjectures found throughout the early literature, did not indicate so much a profundity or acumen, as a well-established tendency to attribute etiological significance to every new clinical or pathological finding. Gairdner in his *Clinical Medicine*, 1862, noted fatty degeneration of the liver as one of the most striking morbid appearances, while the same finding was taken by Perroud (2), earliest of the French school to observe the disease, as the essential causal factor of pernicious anemia.

Biermer's (3) remarkably well-rounded description of the disease contained reference to insufficient and unsuitable feeding, characterizing the lives of many victims, and the persistent diarrhea, anorexia, "weak digestion" and gastric discomfort noted during the disease.

William Hunter's studies, begun in 1885 and published at frequent intervals for many years, are of great importance, especially because they directed attention to features other than the purely hematological. His work on hepatic siderosis manifested an accuracy of observation, then too uncommon. He is responsible for glossitis as a diagnostic sign. Oral infection had been given little, or at best sporadic, thought in connection with any disease until Hunter's tireless descriptions of the mouth conditions in pernicious anemia really laid the ground work for all subsequent ramifications of the concept of "focal" infections in general.

SYMPTOMS AND SIGNS

Without counting achlorhydria, which is virtually constant, the other symptoms and signs referable to the digestive system tract are equally frequent with those of the nervous system and almost as frequent as are the blood changes. Eighty per cent of patients present definite gastro-intestinal manifestations. In view of the fact that over 99 per cent show achlorhydria (indeed, achylia) the digestive tract always is abnormal.

Panton *et al.* (4) have shown that vomiting and diarrhea are the most common symptoms, with anorexia and epigastric pain closely following in incidence. Although these symptoms occur in only 20 to 40 per cent of patients, often they are extremely impressive, especially the persistent diarrhea and the extreme anorexia. Sore mouth and tongue probably do not exceed an incidence of 50 per cent (Minot, 5), although Hunter (6) and more recently Percy (7) would regard it as almost a constant symptom at some stage of each case. Pyorrhea, apical granuloma, and dental caries seem to have an incidence higher than in most diseases.

The Mouth, Its Contents and the Oesophagus: Glossodynia, sore mouth and painful deglutition depend upon glossitis, stomatitis and a reasonably presumed oesophagitis. Barclay's case was a woman nursing her baby and he ordered her to leave off beer and meat and confine herself to slops! Muller (8) found in six out of sixty-two cases a peculiar stomatitis characterized by small whitish ulcers, "the size of a split pea" on, and under the tongue, very resistent to local treatment, disappearing spontaneously or with remissions, but tending to recur without special reason. Quincke (9), Eichhorst (10) and Laache added further reports, showing the commonness of redness and soreness of the tongue, of painful dorsal fissures, the loss of papillae, the excoriation of the angles of the mouth, the smoothness and cleanness of the tongue, the extension of the soreness into the throat preventing the use of hot or hard

food, and an associated loss of taste and sense of smell. Ewald (11) suggested the term "follicular stomatitis".

Hunter (12), as early as 1889, began a long campaign of education of the profession, and his emphasis on the glossitis and the oral sepsis marks his chief claim to be remembered in connection with this disease. He made sections and cultures of the tongue tissues, demonstrated mucosal and muscular atrophy and recovered a virulent long streptococcus, excellent illustrations of which are to be found in his books. Hunter believed that some specific virus caused the disease, pernicious anemia, and regarded the streptococcus as a preliminary invader of the tongue and of the wall of the entire gastro-intestinal tract, which prepared the tissues for the hypothetical organism.

The glossitis has been sufficiently observed to merit its present position as an important diagnostic sign and one of the specific features of the disease.

The smoothness of the tongue, and its cleanness and moisture prompted Evans (13) to make the striking remark: "A coated tongue and a diagnosis of pernicious anemia is a combination to excite suspicion."

In the most active stage of the glossitis, the organ is fiery red and justifies the common description of "beefsteak tongue". It may be edematous and show indentations along its border from pressure of the teeth. Vesicles filled with serum may occur near the tip on either surface, although this is not common. During phases of marked anemia, the generalized mucous membrane pallor is shared by the tongue, except along the edges, where a mottled redness persists. Simple ulcers, resembling canker sores, may be seen on the tongue borders, on the buccal surfaces of the cheeks or on the anterior walls of the *vestibulum oris*.

Later in the disease, uncontrolled by specific treatment, is to be found the small-appearing "ironed-out" atrophic tongue, with dwarfed or absent papillae, subject still to periodic attacks of marginal redness, but decidedly quiescent. Before the days of specific treatment, this atrophic tongue became a permanent hall-mark of the disease and of similar clinical significance to the permanent macrocytosis, which was to be found even in the longest of the spontaneous remissions. In those days it was abundantly proved that this glossitis resisted all forms of local treatment. It interfered with the taking of nourishment, and not infrequently drove the victim to distraction. It ran in very irregular cycles, being on the whole worse at the beginning and less severe toward the end of the disease.

Glossitis, as Riesman (14) pointed out, often is an inaugural symptom, being present from weeks to even years before the onset of the anemia. There are many patients, however, with atrophic tongues who never remember much active discomfort. Finally, an occasional patient shows a tongue with no glossitis, no atrophy and with no indication whatever of local abnormality.

The cause of the glossitis has long been debated, and for years infection was considered to be responsible. This is by no means logically disproved today, but since the glossitis is one of the very first symptoms to yield to the administration of effective curative material such as liver, it seems to argue for a metabolic etiology.

While it is frankly rare to encounter a patient with pernicious anemia without a foul mouth, since pyorrhea is so very common, nevertheless cases are found with teeth clinically and roentgenographically normal, and, again, other cases develop in individuals long since edentulous. The state of the teeth is important for at least two reasons. Sometimes a severe septic anemia, somewhat resembling pernicious anemia, may result from dental infection *per se:* and, still more important is the fact that pernicious anemia, complicated by infection, was in the past a much more severe disease, and is today much less easily controlled by specific therapy. Doubtless, any severe infection, whether of the teeth or other organs, or whether of acute or of chronic, or focal type, can and actually does help to precipitate pernicious anemia in those individuals constitutionally predisposed thereto.

There is clinical evidence that an oesophagitis similar to the glossitis at times occurs; Schwenkenbecker has described a similar involvement of the nasal mucosa.

Anorexia, nausea, and *vomiting* probably depend primarily on the deficiency known to exist because they disappear very rapidly after administration of liver extract, long before any considerable blood increase is gained. But these symptoms were much worse in pre-liver days in those cases which had the added element of sepsis from teeth or from gall bladders or inflamed appendices, as Hunter (12) and Percy (7) have convincingly demonstrated. Likewise, the symptoms were worse in the instances of benign stenosis of the intestine. Jones and Joyce (15) showed the frequent association between pernicious anemia and cholecystitis. It must not be forgotten too that every case of pernicious anemia probably is a case of chronic gastritis and in this connection, it will be remembered how efficacious HCl proved in treating these particular symptoms.

Epigastric pain variously may be explained on the basis of intra-gastric disease, associated gastro-intestinal conditions or on the basis of an angina pectoris with referred sensation as Coombs has explained at length. Most deceptive when it is of the nature of a girdle pain, arising from the posterior column degeneration, such abdominal crisis has often led to fruitless laparotomy.

Diarrhea of an unusually protracted and intractable type may precede the disease by months or years or may be present for months during the disease. Cornell (16) has described a case in

which ten stools per day for two and one-half years preceded the onset of the recognizable disease. Such diarrhea has a post-prandial tendency but not the decided matitudinal tendency as in sprue. Mucus, pus and even blood may be demonstrated at times in the stools, and there is always much undigested food material. In some cases, great rectal discomfort and sense of burning precede or accompany defecation. The incidence of severe diarrhea before or during the disease is 20 to 25 per cent. It usually causes marked loss of weight. The cause has been variously regarded as (a) rush peristalsis due to the premature opening of the achylic stomach or (b) *B. Welchii* enteritis. While both factors conceivably may be of importance, it is to be noted that the symptom abates after the beginning of specific treatment so rapidly as to suggest that it too is due to the deficiency which liver supplies.

ANATOMICAL AND HISTOLOGICAL CHANGES

Stenosis of the oesophagus has been reported at autopsy, and one of us recently had a case of pernicious anemia associated with an oesophageal stricture, in whom the disease began ten years after he had caused the stricture by drinking lye. He was kept in remission with the most unusual difficulty even on large doses of liver and ventriculin and finally died from a mediastinitis following instrumental dilatation of the stricture.

Fenwick (17) in 1870 demonstrated marked general atrophy of the secretory tubules of the gastric mucosa, but found no evidence of inflammation. There was fatty transformation of the glands, this as the result of a very slow degenerative process, leading to general starvation of the body tissues. Flint (18) supported Fenwick to the extent of admitting that at least some cases of idiopathic anemia, as the disease was then called, depended upon a degenerative atrophy of the gastric glands. Schaumann (19) observed in one case a virtual absence of the stomach epithelium, the remaining glands being few and badly developed, and the mucosa being generally characterized by increase of fibrous tissue, with small sub-epithelial hemorrhages. Quincke (20) found the mucosa of the stomach very thin and the glands few in number, and in a second case a diphtheretic membrane in the colon. Bramwell noted slight intestinal ulceration. Eichhorst (10) felt that any changes found were due to the anemia and of little consequence. However, in one of his cases the mucosa of the intestine, the upper part of the jejunum, the lower part of the ileum, and the entire colon were edematous with small hemorrhages on the edge of the villi.

Nolen (21), from a study of two cases, believed the glandular degeneration to be the cause of the anemia. Nothnagel claimed to show intestinal atrophy in 84 per cent of his post-mortem cases. Pye-Smith (22), in an analysis of 103 cases in 1883, noted the frequent occurrence of fatty degeneration of the gastric glands, occasional leucocytic infiltration between the tubules, and a thickening of the mucosa with parenchymatous atrophy. Henry and Osler's case (23) showed atrophy of the gastric mucosa with complete destruction of the peptic glands over the greater part. Toward the pylorus, atrophy was less marked, but a small-celled infiltration, denoting a chronic inflammation was plainly made out. They said: "A careful study of the case justifies, we believe, the conclusion that a primary atrophy of the mucous membrane does occur, and bears out the suggestion of Flint, Nothnagel and others, that certain of the cases of pernicious anemia depend upon the profound alteration in the gastric tubules." They mentioned the chronic abuse of alcohol in this case as probably a co-operative factor in producing the atrophy.

Lewy (21) thought the same histological picture resulted from ulcerative processes, responsible for the hematemesis in his case. In Kinnicutt's (25) first case, the tubules were absent over large areas, while elsewhere tubular fatty degeneration, hyalin change, and small-celled infiltration were noted, although there was no fibrosis and the sub-mucous coat appeared normal. In his second case the greatest destruction occurred in the deeper portion of the tubules, and was probably caused by a chronic inflammatory process. He could not conceive of these changes as being due to a creeping ulceration. Some cases of pernicious anemia might, in his opinion, be due to the impaired nutrition resulting from consequent functional debility of the stomach.

Rosenheim (26) noted cystic degeneration of the mucosa as well as other evidences of catarrhal inflammation. Hale-White (27), in an analysis of the gross anatomical features in 17 cases from Guy's Hospital post-mortem records, noted in six cases certain abnormalities. In the first case—edematous cecum, two blackish small spots on the mucous membrane, almost diphtheritic in appearance; in the second—numerous ulcer cicatrices in the large intestine, or newly healed ulcers, and a little recent diphtheritic inflammatory exudation in parts; in the third—thickening of the pyloric mucosa; in the fourth—the scar of a small ulcer one foot above the cecum; in the fifth—several scars in the lower part of the small intestine.

Mott's case showed no definite microscopic changes in the stomach wall, although he noted that the mucous membrane was covered by a thin layer of glary mucus. Eisenlohr (28) noted in his case not only gastric atrophy but also *a complete disappearance of glands and villi in the intestine.* He felt strongly that nutritional disturbances consequent on this extensive atrophy caused the disease, and furthermore that the process was one of primary genuine atrophy. Nonné (29) found evidence of chronic inflammation both of the mucosa and the submucosa of the stomach but could detect no glandular atrophy.

Pepper and Stengel (3) as well as Hayem

(31) noted atrophic changes in the stomach, although in one of Hayem's cases, gastritis without atrophy existed. Ewald (11) emphasized the intestinal atrophy in addition to the gastric atrophy, as the obvious cause of the disease. Martius (32) claimed to have noted pronounced atrophy of the intestinal, as well as the gastric mucosa in two of seventeen cases, and adopted the view that the intestinal changes noted were decidedly the more responsible for the disease, and acted by disturbance of food absorption.

Grawitz (33) found gastric atrophy, in one case moderate, in another marked, but was noncommittal as to its significance. Koch found atrophy in both the stomach and the intestine in five cases, thus confirming the observations of Ewald and of Martius, but felt that these findings were secondary to the anemia. Fletcher (34) discovered old inflammatory lesions of the colon, associated with patchy necrosis, hyperemia, and hemorrhages. These he regarded as due to neurotrophic disturbances.

Hunter (35) made similar observations on the occurrence of inflammation and atrophy in the wall of the stomach. Some of his descriptions are graphic as, for example the following:

". . . I found *post-mortem*, marked inflammatory lesions, both old and recent, in the mucous membrane of the stomach. The inflammation was localized and, in certain parts, of the most intense description; the changes in the glandular cells and the infiltration with leucocytes recalled at once the similar appearances frequently presented by glandular structures, like the kidney, when the seat of a localized infection.

"Furthermore, the swollen, pinkish, translucent appearance of the small lymphatic glands, lying on the wall of the stomach itself—under ordinary circumstances scarcely visible to the naked eye—pointed to some recent as well as chronic irritation of the stomach wall itself."

Hunter's conception, which for many years had a great influence, may be summarized briefly as follows: the gastric atrophy was the result of a gastritis due to septic organisms swallowed from the mouth, but the gastric atrophy was neither the result nor the cause of the disease. It was to be regarded as an associated condition. In order to explain the disease, Hunter hypothesized a specific infection by an unrecognized micro-organism for whose successful invasion the septic influence had well prepared the tissues.

As may be surmised from this review, the problem of the gastro-intestinal pathology was in an unsatisfactory state at the close of the last century. Nothnagel, Martius and Ewald all championed intestinal atrophy as the cause of nutritional disturbances which underlay the disease. It remained for Faber and Bloch (36) to detect the fallacy of this argument, by doing away completely with the conception of intestinal atrophy. By injecting 500 c.c. of 10 per cent formalin into the peritoneal cavity immediately after death to preserve the tissues, they found that no atrophy of the intestine existed. What had given the appearance of atrophy was the post-mortem gaseous distention of the bowel. In experiments with dogs they demonstrated how easily this distention might deceive. They showed, moreover, that the intestine in pernicious anemia harbored no inflammation in its wall. This left still unsettled the problem of the constancy of atrophy and inflammation in the gastric mucosa. Faber and Bloch, again using the technique of formalin fixation, showed that while atrophy might or might not exist, chronic inflammation (gastritis) was always present.

The observations of these workers have been confirmed by Lepehne (37). No observations on the intestinal histology should be seriously considered unless the methods of Faber and Bloch are employed. Such methods might do away with some of the more recent alleged findings of intestinal atrophy. Passey (38) has brought the method of biopsy to bear on the problem of the stomach condition. In one case of true pernicious anemia with achlorhydria, a section of the fundus, removed at operation, showed the oxyntic cells fewer than normal, very little atrophy indeed, but definite evidences of inflammation. This bears out the findings of Faber and Bloch, that whether atrophy is present or not, inflammation is always to be found.

The more recent reports on pathological findings in the intestine deal largely with strictures, obstructions, and hypertrophies of the small bowel and with disease of the large bowel. Maynard and Sturton (39) report the case of an individual who nine years before the disease had suffered from colitis, and at autopsy a fine ring of small ulcers was found at a point five feet above the ileocaecal valve. The outer surface of the gut at this point showed a sharp line just as if an end-to-end anastomosis had been performed, although there had been no operation. Microscopically, the mucous layer showed simple ulceration, while the other layers were normal. This ulcerated region caused no constriction of any kind whatever. Coates reports a case which showed at autopsy definite ulcers of the large bowel with a large ileocaecal gland draining the area of an ulcerated patch.

Chapman and Duff (40) in April, 1921, opened the abdomen of a patient on account of a diagnosis of intestinal obstruction. The colon was distended but there was no recognizable cause for the obstruction. A colostomy was done and the patient remained in perfect health until August, 1923, when she returned complaining of dyspnoea, and a diagnosis of pernicious anemia was made. They felt that the pernicious anemia was due to the same toxemia that had caused the paralytic condition of the colon.

Faber reported the first instance of intestinal stenosis with pernicious anemia in 1895. Meulengracht (41) has given particular attention to

these cases of so-called "stricture anemia." In 1921 he reviewed seven cases from his own experience and from the literature. In 1922 he (42) reported a further instance in a woman of sixty-four, with three strictures in a certain segment of the small intestine. Haden (43) has reported a case of clinically typical pernicious anemia occurring with a malignant tumor of the gall bladder and obstruction of the duodenum and colon. He considered it probable that the toxic agent responsible for the anemia had arisen as a result of the stasis or of some alteration in intestinal function, induced by the presence and perhaps pressure of the tumor.

Ross (44) attended a physician who developed pernicious anemia soon after swallowing a sharp piece of lamb bone. The bone lodged in the wall of the ileum and was afterwards passed with the stools, but the patient died of pernicious anemia.

Kleeman (45) reports the finding of simple pyloric hypertrophy in pernicious anemia. The case was operated upon for a schirrhous growth of the pylorus. Percy (7), who has operated upon more cases of pernicious anemia than anyone else, stated, in reply to a question by Gibson, that in seventy-seven laparotomies in this disease he had never encountered pyloric stenosis.

Mayo (46) has noticed the frequent development of a severe anemia, sometimes indistinguishable from pernicious anemia, in disease of the colon, particularly of the proximal half.

Whereas, a few instances of pernicious anemia show various abnormal conditions of the intestine, such as those just described, most cases do not present such findings. Surgeons will agree that similar abnormalities are frequently found at laparotomy without any associated picture of pernicious anemia. The obvious inference is that such abnormalities are not essential but may be contributory, in some way, to the development of the disease.

To sum up—it is recognized that atrophy of the gastric mucosa may or may not occur; that gastritis always occurs; that intestinal atrophy and infection are not proved and much doubted; and that a few cases show stricture, ulcer, or neoplasm of the bowel.

In summing up the information available on the subject of achlorhydria in pernicious anemia, in 1927, one of us (16) wrote: "Achlorhydria, a functional abnormality of constitutional origin, is almost invariably associated with pernicious anemia, and forms, in these cases, a necessary link in an etiological chain, to which, by the addition of *further unknown* links, pernicious anemia is made to appear." While the latter part of the present monograph will reveal how true that statement was, it is considered wise, at this point, to present the reader with some of the extensive background of investigation responsible for the 1927 attitude.

Grawitz in the late nineties listed "achylia gastrica" as a definite etiologic factor in the broad group of cases which he, in conformity with continental custom, included under the term, "pernicious anemia". Faber and Bloch (36) collected 33 cases of the disease in which gastric analysis had been done, and in all of which the acidity was greatly diminished or absent. Similar results were obtained in their own four cases, and *post-mortem* examination showed diffuse inflammation of the stomach wall with destruction and atrophy of the glands. Faber maintained for many years that the gastric changes and the blood changes had a common cause in a general toxic-infective state of the body, though he finally came to view the achlorhydria as possibly a constitutional manifestation.

Hutchison (47) in 1909 demonstrated that since achlorhydria so often existed for years without blood changes, it could not, *per se*, be validly regarded as the cause of the disease. He admitted that achlorhydria robbed the intestinal tract of its natural antiseptic and was among the first to recommended HCl as a rational method of therapy.

The report of Levine and Ladd (48) of finding achlorhydria in 99 per cent of 150 cases of pernicious anemia was the first of a series that eventually settled the importance of the finding. Hurst (49), Faber and Gram (50), Percy (7), Panton et al (4) all made similar studies with identical results. Hurst and Bell (51) found achlorhydria to be as characteristic of "pure" cases of subacute combined degeneration of the spinal cord without anemia, as of the cases showing anemia, and their report did more than any other to unify the conceptions of neurologists with respect to this disease. Piney (52) found one case of subacute combined degeneration of the cord with free HCl present, just as Shaw, and others more recently have done in cases with anemia. These exceptional instances proved stumbling blocks to constructive hypothecation along etiologic lines until quite recently, as will be shown later.

Faber and Riley (53), Hurst and others (54), (55), (56), (57), (58), were able to show definitely that achlorhydria preceded the disease in all cases where the point could be settled, for periods of from one to twelve years. The condition of achlorhydria was more permanent than the disease, for in the instances of 20-year spontaneous remissions of Hurst's, the HCl never appeared. Achlorhydria, when not associated with pernicious anemia, often shows some degree of recoverability as in alcoholic cirrhosis or cirrhosis of the liver, but in pernicious anemia it is consistently persistent.

At first the anemia itself was regarded as the cause of the achlorhydria, and then a toxic-infective or "noxa" factor was accredited with producing a parenchymatous gastritis or perhaps an interstitial infectious gastritis which, by gradual condensation of fibrous tissue, resulted in eventual atrophy of the secreting cells. Finally the idea of achlorhydria being a constitutional, and

even an inherited, characteristic has gained so much ground that it is practically accepted today. The biopsies of Hurst and Passey proved that the gastric mucosa in pernicious anemia may be histologically normal although achlorhydria was present. The occurrence of *familial* pernicious anemia, and the high incidence of achlorhydria in close relatives of patients with the disease supports the constitutional conception.

Much recent work on achlorhydria, itself, has shown it to be much more prevalent in the general healthy population than formerly believed, and to follow, in its incidence certain age levels. Perhaps it usually causes no symptoms whatever, or at most, predisposes to diarrhoea and an absence of alkaline tide in the urine.

THE FOOD FACTORS

Much experimental work on anemias due to vitamin deficiency has been undertaken, but no reproduction of a condition resembling human pernicious anemia has been accomplished.

The voluminous work on vitamins during the past decade unquestionably suggested that avitaminosis might play some role in pernicious anemia. Falconer concluded that blood changes in vitamin A deficiency were neither striking or constant enough to constitute specific deficiency lesions. Koessler *et al.* (59) do not indicate the condition of pigment metabolism in the anemia they produced in rats by chronic vitamin A deficiency and, hence, any comparison with pernicious anemia, lacking this information, is problematical. They indicate that in this experimental anemia, produced by vitamin A deficiency, blood regeneration occurs only with, and in proportion to, the addition of vitamin A. Nothing could appear more logical, since no anemia can improve so long as the set of conditions responsible for the anemia do not change. Simmonds *et al.* (60) suggest that Koessler's rat anemia was due to deficiency in vitamin E, which is believed to play an important role in the absorption of iron. Whatever may have caused the anemia, it does not, from their description, appear to bear any necessary relationship to pernicious anemia; and in fact Koessler *et al.* propose such a vitamin A deficiency not as a sole, but rather as a co-operative factor in the etiology of the human disease.

Barker and Sprunt (61) emphasized the importance, on general principles, of treating pernicious anemia by liberal and well-balanced diets. Many others have, with no recognizable specific reason of importance, advised special diets of various kinds. Mosenthal (62) showed that forced feeding can restore a positive nitrogen balance. Gibson and Howard (63) showed in careful metabolic experiments that more favorable nitrogen and especially iron balances may be established in pernicious anemia when diets rich in food iron, and comparatively low in caloric and protein values are given, and urged the use of iron-rich and vitamin adequate diets in the treatment of this disease. This was an intentional, clinical application of high food iron diets which had been found by Whipple *et al.* (64, 65) so valuable in causing blood regeneration in dogs rendered anemic by hemorrhage. Elders (66), fully convinced of the possibility that sprue and pernicious anemia possess a common etiology, and equally convinced that sprue is a deficiency disease, suggested that pernicious anemia might be found at least amenable to improvement by well-chosen food. Minot and Murphy (67) found it permissible to speculate "on the possible partial *rôle* that some nutritional excess or deficiency may play in the etiology of the disease". With a special diet rich in proteins of good biological value, particularly liver, low in fat and carbohydrate and with vitamins well supplied, these investigators obtained remarkable therapeutic results, more constant and more lasting than those obtained by any other form or forms of treatment. The published work of Minot and Murphy brought the whole problem of nutrition in pernicious anemia to a sharp focus of interest. Their results suggested the possibility that dietary factors may actually play a *rôle* in the production of the disease. No studies of the pre-disease diets of patients had as yet appeared.

In 1927, Cornell showed by a study of the pre-disease diets of twenty-five persons, later developing pernicious anemia, that it was not a true deficiency disease in the ordinary sense of the term because these individuals, prior to their disease, had regularly eaten diets which could be regarded as of average type.

BACTERIA AND PARASITES

As might be expected, most of the intestinal bacteria and most of the parasites occurring in the stools of patients with pernicious anemia have received rather extensive study. The streptococci, *B. Welchii*, and *B. Coli*, have all been formally suspected of causing the disease. Hurst, in England, led the streptococcus hypothesis, receiving the mantle from Hunter. Herter (68), of New York, in 1906, initiated the *B. Welchii* hypothesis followed years later by Cornell (69), Kahn and Torry (70), Reed, Orr, and Burleigh (71) and others. Adami (72) in Montreal in 1900 started the "subinfection by B. Coli" conception and further work on this phase was done by Lowenberg (73), Percy (7) and Nyfeldt (74).

(To Be Continued)

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ABSTRACTS

JOSLIN, E. P., AND LAHEY, FRANK H.

Diabetes and Hyperthyroidism. Ann. Surg., October 1934. Boston, Mass.

The authors stress the fact that glycosuria is so related to hyperthyroidism that care must be taken not to make the diagnosis of true diabetes in hyperthyroidism when it actually does not exist. Raised blood-sugar levels are suggested to avoid this common error. Dr. Lahey states that the important part of the successful care of diabetes and hyperthyroidism is the management of the diabetes.

The authors believe that the combination of diabetes with hyperthyroidism increases the risk and, therefore, demands more conservative operative approach if the mortality is to be kept low.

Attention is called to the need of avoiding unnecessary puncture for laboratory tests of the superficial veins in patients with hyperthyroidism and diabetes. As a means of avoiding such punctures, the employment of capillary blood from the ear, and the use of micro blood-sugars is suggested.

A conclusion is made that the effect of hyperthyroidism on diabetes is to intensify the disease, as with infection, increasing the demands for insulin. It would appear that diabetes has no effect on the hyperthyroid state except definitely to increase the surgical risk.

Following the surgical relief from hyperthyroidism there is an increase in carbohydrate tolerance of 30 gms. or more, and a marked diminution in the need for insulin.

Charles R. Sturgeon, Los Angeles, California.

CHURCHILL, EDWARD D.

The Operative Treatment of Hyperparathyroidism. Ann. Surg., October, 1934. Boston, Mass.

A classification of diseases of the parathyroid glands is proposed that differentiates generalized hyperplasia from single or multiple adenomas. The principle of subtotal resection in the operative treatment of hyperparathyroidism finds application in both types of the disease, but particularly in generalized hyperplasia associated with hyperparathyroidism.

The author presents twenty-one cases of proven hyperparathyroidism all going to operation. Three of these cases were generalized hyperplasia of the glands associated with hyperparathyroidism. Eighteen cases showed typical adenoma of one or more parathyroid glands associated with hyperparathyroidism.

The author repeatedly warns against the removal of normal parathyroids when a diagnosis of hyperparathyroidism has been established. It is advisable to do a subtotal resection of a large single adenoma in patients who give evidence of a depleted calcium and phosphorus reserve evidenced by general skeletal decalcification. The goal of subtotal resection is to correct the state of hyperparathyroidism by reducing the total amount of functioning tissue to that amount consistent with a normal calcium and phosphorus metabolism.

One gathers from this article that it is far better to err on removal of too little parathyroid tissue than to be too radical and do complete removal with resulting serious tetany. Charles R. Sturgeon, Los Angeles, California.

MIXTER, CHARLES G., BLUMGART, HERRMAN L., AND BERLIN, DAVID D.

Total Ablation of the Thyroid for Angina Pectoris and Congestive Heart Failure. Ann. Surg., October, 1934, Vol. 100, Pages 570-575. Boston, Mass.

Seventy-five patients suffering from angina pectoris or decompensated heart disease have been subjected to total ablation of the thyroid gland. The authors state that the procedure is no way curative and the underlying lesion of the heart is not rectified.

In general the authors feel that the operative treatment of properly selected patients with angina pectoris has been of definite value. It was evident early in the investigation that the permanent beneficial effort of thyroidectomy is not to be expected until the basal metabolic rate has fallen 20 per cent or more. The time required to reach this level is about four weeks after operation.

Fifty patients suffering with congestive heart failure were operated upon, with a 12 per cent mortality, however, no death has occurred in the last twenty-two consecutive cases. Fifty-five per cent of cardiac patients formerly incapaciated and confined to bed a great part of the time are now working or able to work.

Patients with congestive heart failure who have evidence of rapidly progressive heart disease, in spite of all available medical procedures can expect only temporary improvement from thyroidectomy. Four patients with a history of coronary thrombosis, experienced little or no relief after operation.

Regardless of the pre-operative metabolic rate, all patients required the administration of small doses of thyroid to control signs and symptoms of myxedema when the metabolic rate reaches approximately minus 30 per cent. The presence of a low pre-operative basal metabolic rate represents a definite contra-indication to operation.

The authors attribute their marked decrease in mortality in their last series of twenty-two patients, to improvement in medical management of these patients as well as to the rise of local anesthesia and increasing surgical experience.

Charles R. Sturgeon, Los Angeles, California.

Medical Aspects of Peptic Ulcer with Special Reference to Diagnosis and Treatment

By

ARTHUR F. CHACE, M.D.
NEW YORK CITY, NEW YORK

PEPTIC ulcer, a common affliction occurring in all races and under the most diverse conditions of life, is a systemic disease. Owing to improved methods of diagnosis, particularly radiological technic, its recognition has become more frequent than formerly. It is one of the few diseases which, in spite of the great strides which have been made in preventive medicine, is becoming more prevalent.

Peptic ulcer represents a maladjustment to one's environment. Certain factors in the modern mode of living predispose to the formation of peptic ulcer. The unnatural *tempo* to which everything about metropolitan life is speeded, hasty eating often in the tense atmosphere of business discussion instead of the leisured relaxation of continental dining, all have this most unfortunate effect of peristalsis on the lining of the stomach. Many of these factors are known to us all, but disregarding this knowledge, we continue to suffer from ulcers. I say "we" because physicians are probably more prone to have peptic ulcers than any other group in the community.

Individuals with an orthotonic type of body, with overactive thyroids or adrenals, an unbalanced vagus and sympathetic nervous system, or with arterial disorders particularly are likely to have ulcers. That focal infections play an important secondary role in the causation of ulcer definitely has been established.

The question why the stomach is not digested by its own gastric juice is an interesting one. The mucous membrane is probably protected by a hormone, but any injury to the mucous membrane, bacterial or toxic, diminishes its resistance to hydrochloric acid and pepsin. Ulcers occur most frequently in that portion of the duodenum and stomach which is exposed to the most concentrated acid chyme.

Patients with peptic ulcer frequently complain of the symptom syndrome popularly known as "dyspepsia", *i. e.*, eructations, pyrosis, feeling of fullness after meals, nausea, capricious appetite, headache and incomplete evacuations of the bowels. These symptoms are of very slight diagnostic value as they may occur in any lesion of the digestive tract. The most indicative symptoms are *pain, vomiting and hemorrhage.*

The *pain* is gnawing in character, located in the epigastrium, and usually radiates to the back. It is periodic and bears a definite relationship to meals. The time of occurrence depends upon the location of the ulcer. The pain is relieved by bland foods or by alkalies, and is aggravated by irritating or coarse articles of diet. "Hunger pain" often comes on after midnight and is relieved by food or alkalies. Attacks of pain of a few days' duration alternate with a few days of complete euphoria. During the periods of remission, patients have a false sense of security. The alteration of relief and attacks is very characteristic.

Patients with small ulcers, particularly of the duodenal type, rarely suffer from *vomiting.* When vomiting does occur, it is due to the closure of the pylorus, either from organic disease or from spasm. The patient is afforded great relief by the emptying of the stomach.

Hematemesis occurs in relatively few cases of gastric ulcer, and melena is found in about 25 per cent of the cases of duodenal ulcer. The finding of occult blood in the feces is the rule in most cases of peptic ulcer, *i. e.*, at the time when the ulcer is "active".

It must be remembered that the majority of patients with peptic ulcer do not vomit or have hemorrhages, and that a small minority escape distress and attacks of pain.

On *palpation* one usually notes slight rigidity of the right rectus muscle, sometimes of the left rectus, depending upon the location of the ulcer. This sign is associated with tenderness on deep pressure. A mass is only felt in cases of inflammatory exudate around the ulcer, or due to proctected perforation of varying extent. Zones of

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skin hyperesthesia in the epigastrium and along the spine are of minor significance.

The most *important laboratory aid* is the finding of occult blood in the feces. The patient should be on a strictly blood-free diet for at least three days before the stool test is made. Analysis of the *gastric contents* after an Ewald test meal or the determination of the amount of hydrochloric acid by fractional methods is a valuable aid to diagnosis. Test meals to determine the motility of the stomach and to estimate the potency of the pylorus are useful, but these methods have been somewhat superseded by the Roentgen ray.

The roentgenologist furnishes the most positive evidence of peptic ulcer: the *direct findings* of a niche, filling defects and irregularities in the mucous membranes; the *indirect findings* of abnormal motility and of pylorospasm. It is important when using the fluoroscope to observe the patient when he is in different positions.

The *diagnosis* of peptic ulcer is difficult, but if advantage is taken of all the means at our disposal it can be made with a great degree of certainty, even in perplexing cases. The impressions obtained by taking a careful history are most suggestive; the attacks usually can be traced to definite causes and are temporarily alleviated when these causes are removed. The periodicity of the pain, its relationship to meals, and its relief by alkalies are almost pathognomic of certain peptic ulcers. The evidence obtained by abdominal palpation is contributory, but not so significant. The laboratory findings of gastric acidity and of occult blood in the stools aid in the diagnosis; positive X-ray evidence makes it certain.

DIFFERENTIAL DIAGNOSIS

The whole problem of differential diagnosis is simplified tremendously by the X-ray. Peptic ulcer must be differentiated from nervous conditions, both functional and organic, from gastritis, duodenitis, duodenal adhesions and diverticula, gall bladder disease, reflex disturbances with gastric symptoms, from appendicitis and other intestinal conditions. Such rare conditions as syphilis and tuberculosis of the stomach also should be considered. The distress of a small epigastric hernia will sometimes simulate that arising from ulcer. The pain from such a hernia often causes the patient to diagnose his own case as ulcer, but the physician's discovery of the hernia establishes the true diagnosis.

The subjective symptoms of the nervous dyspepsias can imitate almost exactly those of ulcer, but careful analysis of each individual patient shows that the pain in the neuroses does not have the characteristic relationship to meals. The absence of occult blood in the feces together with negative X-ray findings rule out ulcer.

The gastric crises of *tabes dorsalis* accompanied by severe attacks of vomiting and pain, suggest the possibility of ulcer, but the positive, classical signs and symptoms arising from a spinal cord lesion considered with radiological findings negative for ulcer, make the diagnosis of *tabes dorsalis* definite.

The more recent technic of studying the *rugae* of the stomach intensively by X-ray after the patient has taken a dram of barium, instead of the former eight- or ten-ounce dose, enables one to differentiate readily between gastritis and peptic ulcer. This technic brings out more clearly the swollen and tortuous ridges of the mucous membrane and also reveals any pathological signs of ulcer. The same type of radiological study also is of value in differentiating between duodenitis and duodenal ulcer.

Furthermore, radiography enables one to visualize the position, size, shape and activity of the duodenum, and shows clearly diverticula or duodenal adhesions. The examination of the duodenal contents by means of the duodenal tube is an aid in determining the extent of the interference with the normal peristaltic movement of the duodenum.

The symptomatology of *duodenal stasis* due to adhesions, diverticula and bands, is not definite. The pain does not bear a definite relationship to meals, although the patient is relieved of distress when the duodenum is emptied. These patients exhibit the symptoms of dyspepsia which are common to all abdominal conditions.

Cholecystitis, with or without cholelithiasis, is easily recognized by X-ray; but mild cases of cholecystitis produce reflex gastric symptoms very similar to those of peptic ulcer. In fact it is this type of case which demands the greatest diagnostic acumen. A careful study will show that the pain in uncomplicated ulcer is more periodic, bears a definite relationship to meals and is relieved by bland food and alkalies. In ulcer cases, occult blood is found in the stool. Examination of the contents of the duodenum or of the gall bladder, obtained through a duodenal tube, is of great assistance in differential diagnosis. In gall bladder disease, the bile contains a large number of bacteria, desquamated epithelial cells, leukocytes and cholesterin crystals. The use of the *dye test,* sponsored by Graham and his associates, for the study of the gall bladder is most helpful. The clinical picture is made less clear when there exist adhesions between the duodenum and the gall bladder.

In a group of cases, duodenal ulcer and disease of the gall bladder coexist (approximately 18 per cent).

Chronic appendicitis reflexly can cause spasm of the pylorus which will produce nausea, vomiting and pains; in atypical ulcer cases, appendiceal gastric irritation makes it difficult to distinguish the lesion from peptic ulcer. Differential diagnosis particularly is difficult in retrocecal appendices since then the pain and tenderness may be in the region of the duodenum. Pain constantly present in the right, lower abdominal quadrant or

in the right flank, on deep pressure is the most characteristic evidence of chronic appendicitis. If this sign is associated with X-ray evidence of retention of barium in the appendix, the diagnosis of appendicitis is assured.

The radiological evidence is the most valuable aid in the differential *diagnosis between carcinoma and ulcer.* All doubtful cases early should have such an examination before, if cancer exists, it is too late successfully to perform operative procedures. However, when histories are carefully taken and interpreted, the symptomatology is strikingly different. Carcinoma comes on so insidiously or so rapidly with few symptoms that the early phases of disease entirely may be overlooked. In ulcer cases, the use of the stomach tube following a test meal will reveal varying amounts of acidity, but practically never anacidity; whereas in the presence of even moderately advanced carcinoma, lack of hydrochloric acid is the rule.

Syphilitic ulcer of the stomach is a rare condition; its symptomatology is more like that of cancer than of ulcer. The onset is insidious. Patients who give positive Wassermann reactions not infrequently are affected with peptic ulcer. However, it should not be assumed that because there is a positive Wassermann reaction, the ulcer present is luetic in etiology.

Tuberculous ulcer of the stomach is exceedingly rare. Its symptomatology may resemble that of cancer.

TREATMENT

The treatment of peptic ulcer should be adapted to the specific needs of each patient. Not only should the type of ulcer and its location be determined, but all the factors—constitutional, emotional and local—which may have, in any degree, entered into the ulcer's causation, should be considered. It is important to remove all foci of infection, the more common sources of which lie in teeth, tonsils, nasal accessory sinuses, gall bladder, appendix and genito-urinary tract. The basal metabolism should be determined and any endocrin inbalance corrected.

The patient should be examined thoroughly for any evidences of constitutional disease which might lower the tone of his general health. Influences which diminish the resistance of the mucous membranes should, so far as possible, be eliminated.

An estimate of the patient's resistance to ulcer-formation, the "virulence" of the ulcer itself and the tendency to recurrence should be taken into consideration.

The treatment should be highly individualistic. An understanding of the emotional life of the patient frequently will show disharmonies, phobias, anxieties, and maladjustments, and a tense attitude toward the problems of daily life. Disordered emotions have a profound influence on the autonomic mechanisms of the body, particularly in producing irregular peristalsis. Nothing interferes more with the healing of peptic ulcers than hyperperistalsis with pylorospasm. Disorders of secretion go hand in hand with disorders of motility. The hyperacidity so characteristic of peptic ulcer is controlled in a large measure through the nervous system. The emotional life of the patient must be restored to normal in order to balance the impulses flowing over the vagus and the sympathetic system. Patients must be taught to develop equanimity of spirit and to evolve a philosophy of life suited to their individual needs.

The establishment of a definite *regime* with adequate time for sleep and mental and physical relaxation is imperative. This can be accomplished much more satisfactorily in an institution where the patient can be protected from the petty annoyances of life than is possible in his own home. Rest in bed, with the application of hydrotherapy and thermotherapy, is one of the most effective means of producing relaxation. Various modifications of the original Preissnitz dressing are efficacious. Small doses of one of the nerve sedatives are useful in controlling purely nervous symptoms and in decreasing vagatonia.

The *diet* should be balanced as regards the proportion of carbohydrates, fats and proteins, and should supply the caloric needs of the patient. In arranging a dietary which is mechanically non-irritating, one should keep in mind its vitamin, mineral salt and anti-scorbutic content. Parenthetically speaking, it might be added that the patients occasionally develop scurvy on rigid, sterilized diets. Ulcer patients usually are unable to take fresh fruit juices owing to their irritating effect on the mucous membranes. The anti-scorbutic element may now be added to the diet in the non-irritating form of crystalline vitamin C (ascorbic acid). Its use particularly is valuable in cases with a tendency toward bleeding.

Milk, owing to its bland character and its property of combining with hydrochloric acid, is the basis of the diet in early treatment of ulcer. If milk gives distress, due to the too rapid formation of curds, ten to fifteen grains of sodium citrate may be added to each three- to four-ounce feeding. Milk also may be made more digestible by mixing it with strained cereal gruel, malted milk or arrowroot. If milk remains too long in the stomach, carbohydrates in the form of gruels made of rice, barley or cream of wheat may be alternated with or substituted for it. Cream may be added to the milk to increase its caloric content, but care must be taken not to overburden the liver by so doing.

An effort should be made to keep the content of the stomach alkaline by giving hourly feedings from the time the patient awakens in the morning until he goes to sleep at night. If he awakens during the night, an additional feeding is given. It is important that the diet be palatable and take into account the patient's idiosyncrasies. Those subjects who cannot tolerate milk are given four to five ounces hourly of cereal gruel with the addi-

tion of one or two soft boiled eggs during the day. Variety may be obtained by substituting arrowroot, custard, junket, plain cornstarch puddings or malted milk. It is well to add one or two feedings of a half ounce of olive oil during the day as it inhibits the secretion of acid and, in most cases, is soothing to the stomach.

During the *second week* of management the patient usually can tolerate toast Melba, unsalted butter, *potages* made with well-cooked cereal with cream added, and thoroughly puréed vegetables. The caloric values of the food rapidly may be raised by increasing the amount of cream, unsalted butter and olive oil. During the *third and fourth weeks*, finely minced chicken, fish, lamb chops or sweetbreads may be given once a day. Although hourly feedings are prescribed, it is customary to omit one of the milk and cream feedings, particularly the one following a meal in which meat has been given.

In a very few cases, it is possible to keep the stomach alkaline by diet alone. Usually, however, it is necessary to give alkalies one-half hour after each feeding. A mixture of five grains each of sodium bicarbonate, calcium carbonate and magnesium carbonate agrees with the patient better than any one of these drugs given separately.

Patients on a diet which has a low salt content, develop *alkalosis* rather quickly when taking alkalies continuously, especially if in addition to their ulcers they have renal insufficiency. The early symptoms of alkalosis are drowsiness, vertigo, and headache. The later symptoms are embarrassed breathing, slow pulse and coma. Examination of the blood reveals an increase in the carbon dioxide content of the blood and urea, with a corresponding loss of blood chlorides. This leads to an increase in the pH in the blood. The condition of alkalemia clears up promptly when alkalies are stopped and chlorides are administered by mouth or intravenously. Rarely is it necessary to give hydrochloric acid or ammonium chloride. If there is any tendency to alkalosis it is wiser to control the acidity by administering either bismuth subnitrate, bismuth subcarbonate, aluminum silicate or aluminum hydroxide instead of the commonly employed antacids. The preparations of aluminum may be given together.

In order to overcome the disadvantages of the alkalies, *mucin* has been extensively used in the treatment of peptic ulcer. It is soothing to the stomach and neutralizes gastric acidity. It has been given in doses amounting to one hundred grams a day. However, generally, the results of its use have been rather disappointing. It is unpalatable to many patients in spite of efforts to disguise its taste. In patients with kidney disease complicating peptic ulcer, it has been shown to produce an increase in the blood urea.

In some cases preparations of belladonna, atropine or hyacyamus may be used with great efficacy in controlling hypersecretion and hypermotility. These may be given regularly or as symptoms demand during the discontinuance of alkaline feedings. A small dose of atropine sulphate, at bedtime, will inhibit the secretion of gastric juice during the night. The bowels may be regulated by giving an emulsion of mineral oil and agar agar.

Subcutaneous and intravenous injection of vaccines, serums, non-specific proteins, salts of hystidine, emetine and other drugs have been used to hasten the healing of ulcers and to increase the resistance of the patient to ulcer formation. These procedures do not take the place of the established methods of cure, and, if used at all, should be supplementary. The injection of non-specific protein inhibits peristalsis and in this way, particularly when combined with the proper diet, relieves the patient's distress. If a patient obtains relief under the inadequate, ambulatory treatment, he is satisfied, but stops short of being cured, with the result that the condition recurs as soon as he returns to his old habits of eating and living. It is essential that ulcers should be thoroughly cured by strict dietetic *regime* in order to avoid future trouble.

Complete rest of the stomach may be obtained in certain cases of gastric ulcer by feeding the patient with a milk and carbohydrate mixture through a small tube directly into the duodenum. This method has been successfully used; but no matter how carefully performed, the presence of the duodenal tube is a nervous and physical irritant to the patient.

The degree of alkalinity or acidity of the gastric contents may be ascertained by aspirating through a small tube. The stomach also may be aspirated at night in the hope of avoiding an accumulation of acid when the feedings are discontinued. This method is a guide to the amount of alkalies to be given. It is advisable to avoid the use of the tube whenever possible and to be guided rather by the patient's symptoms. The disappearance of symptoms, the absence of occult blood in the feces and negative X-ray findings are conclusive proofs of the healing of the ulcer.

Management of Ulcer Complications: As *hemorrhage* is the most frequent complication in peptic ulcer, occurring in about 25 per cent of the cases, its treatment deserves especial consideration. In duodenal ulcer, hemorrhage into the bowels sometimes is the first positive evidence of ulcer. Before the blood appears in the stool the patient suffers from colicky pains and faintness. The blood pressure drops suddenly and the hemoglobin is reduced in proportion to the amount of blood lost. The patient should be kept absolutely quiet with an ice bag over the epigastrium, and a hypodermic of morphine with atropine given. Nothing should be taken by mouth for two or three days. Dehydration can be prevented by retaining enemas of saline and glucose solution. If the hemoglobin drops below 50 per cent, small transfusions of blood are indicated. Two to three days after the hemorrhages have stopped, small

amounts of milk, alternating with alkalies may be used and the patient gradually placed on the regular ulcer *regime*. Death from hemorrhage is extremely rare in ulcer cases.

The treatment of *perforation* is entirely surgical, but its early recognition by the medical man is imperative. Excruciating epigastric pain with prostration, sweats, rapid, shallow respirations, sub-normal temperature and weak pulse, followed by rigidity of the abdominal wall are so characteristic of perforation to any trained physician that when such crisis arises a surgeon should be summoned immediately.

Continuance of Ulcer Therapy: A dietetic rest regime of four to five weeks is necessary for the proper healing of peptic ulcer. Although the symptoms usually disappear after the first week of rest in bed, occult blood may continue to be found in the stool for two or three weeks. Owing to freedom from discomfort the patient has a false sense of well-being; this results in impatience and the desire to discontinue institutional care often before X-ray studies demonstrate that the ulcer actually is healed.

The high incidence of *recurrent peptic ulcer* is due to incomplete cures. After the patient leaves the hospital with a healed ulcer he should follow a modified dietetic regime for at least a year. He should be warned that the mechanisms which produced the original ulcer, still are operating and if not avoided, will be responsible for recrudescence of the original ulcer or the development of a new one. He should avoid coarse and irritating food, condiments, sweets and those articles of diet which stimulate gastric secretion. Tea, coffee, alcohol and tobacco should be interdicted. The use of tobacco particularly is harmful, especially to susceptible subjects, in that it interferes both with the secretory and motor functions of the stomach—probably by disturbing the balance between the vagus and the sympathetic system.

The meal hours should be free from nerve stress; food should be thoroughly masticated. The gastric acidity can be controlled by taking a glass of milk, modified as described above, in mid-morning, mid-afternoon and at bedtime. The patients should have a complete health examination at least every six months, with a view to correcting any tendencies which might lead to ulcer.

In conclusion, let me emphasize that peptic ulcer is a *constitutional* dyscrasia, associated with a *local* lesion in the digestive tract; that its incidence greatly can be reduced by preventive measures; that it can be cured and its recurrence controlled by the application of knowledge obtained through a detailed and individualized study of each subject.

ABSTRACTS

DUGGAN, C. E.

Staphylococcus Antitoxic Serum in the Treatment of Acute Staphylococcal Infections and Toxaemias. Can. Med. Jour., June, 1934, p. 601.

Staphylococcus antitoxic serum has been prepared before in Germany and in England and the beneficial results of its use reported. It has been prepared in the Connaught Laboratories in Toronto and for two years has been available for clinical trial.

Bacteria free staphylococcus exotoxin was prepared from a strain of high toxicity; this was first treated with formalin (toxoid) and injected with increasing doses; later crude toxin was used. In this way a high titre of antitoxin was obtained and the high fatality to the horses reported by previous workers was avoided. The serum was concentrated, 0.2 pc. tricresol added, and prepared for distribution in 50 c.c. quantities.

The serum prepared in this way neutralized in a marked degree the pathogenic effects of the toxin. The dermonecrotic effects are neutralized and the leucocidin substance which destroys the phagocytes which are the chief defense against staphylococci, is also neutralized. On the other hand, a plasma-coagulating substance, which has been inhibited *in vitro*, by other workers, has not yet been satisfactorily neutralized.

Summing up, the authors say that a serum has been obtained which neutralizes the toxin or toxins which cause the pathology of staphylococcus infection. One hundred and four patients with various staphylococcus infections, all confirmed by bacteriological examination, were treated. These included carbuncles, skin conditions, arthritis, empyemas, pyaemias, osteomyelitis, many of whom had positive blood cultures. Treatment was by serum in large doses, mostly intramuscularly, as the intravenous route gave very severe reactions. This was followed in suitable cases by injection of the toxoid. Improvement became definite when the anti-haemolytic titre of the patient's serum rose, and often this was accomplished by leucocytosis. Emphasis is laid on the importance of early diagnosis, and prompt institution of specific antitoxic treatment especially where a careful blood culture shows staphylococci, a finding that has so often been ignored in the past as representing a contamination.

Although 39 of the 104 cases so far treated died, the author feels, as he very modestly concludes, that with staphylococcus antitoxic serum they have a therapeutic agent of very considerable usefulness.

SECTION VI—*Abdominal Surgery*

Diseases of the Pancreas, Especially Acute Pancreatitis and Its Treatment*

By

JOHN DOUGLAS, M.D.
NEW YORK CITY, NEW YORK

SURGICAL lesions of the pancreas are not sufficiently common for any one surgeon to see a large enough number and so to form definite conclusions from his personal experience. Such lesions do occur, however, with enough frequency to make it necessary for the general practitioner at least to suspect that the pancreas may be the cause of the symptoms, particularly in the presence of an acute abdominal catastrophe.

In order to make up for the lack of a large personal experience, a study of the literature and an examination of the histories of a group of cases from a large hospital help to clarify one's ideas. But, in the literature, one meets with many differences of opinion, and, in the case histories, a study of the pathological condition found at the time of operation compared with that found in subsequent autopsy reports further may confuse one's ideas. Even the nomenclature of the disease is a subject of confusion. The lesions variously are reported as "acute pancreatitis", "acute pancreatic necrosis", "acute hemorrhagic pancreatitis", "subacute pancreatitis", "edema of the pancreas" or even "chronic pancreatitis". No one diagnosis covers all cases, and chronic pancreatitis is included here because what appears to be a minor or chronic lesion of the pancreas may be found at an operation for cholelithiasis or cholecystitis. Then, after what is believed to be the proper surgical operation, should the patient die within a few days, a most severe form of necrosis or disintegration of the pancreas may be found at autopsy.

DATA FROM THE LITERATURE AND HOSPITAL RECORDS

On examining the literature, one finds very little reduction in the mortality over a period of years. In 1911, Korte reported one hundred and three cases with 60 per cent mortality. In 1927, Schmieden and Sebening tabulated one thousand two hundred and seventy-eight cases with fifty-one and two-tenths per cent mortality. A statistical study of this condition, however, would appear to be of somewhat questionable value because of the various types of lesion included in such a group of cases. In a review of the histories of the cases operated on for acute surgical lesions of the pancreas at St. Luke's Hospital, this difficulty was made most apparent. Many of the cases were operated upon with the diagnosis and in the presence of acute gall bladder lesions and a certain degree of pathology of the pancreas was found, frequently no more than a thickening of the head of the pancreas with some fat necrosis about the gland. Several of these patients died, and at autopsy it was found that the pancreatic lesion had extended even to a degre of almost complete pancreatic destruction; this had been the cause of death. Thus, the mortality rate would depend on the type of case on which operation was performed. In a series of thirty cases operated on in St. Luke's Hospital during fifteen years previous to 1933, there was a 50 per cent mortality. Since that time, there have been six operative cases with only one death, but the fatal case was the only one in which an acute fulminating lesion was present.

ETIOLOGICAL CONSIDERATIONS

In the study of the etiology, conflicting facts, or observations which have been interpreted as facts, should be considered with relation to each other. Such consideration may demonstrate the reasons for the conflicting theories. Seventy-eight years ago (1856), Claude Bernard proved, experimentally, that, in animals, the *injection of certain substances into the pancreatic duct* would cause death from, or various degrees of, acute pancreatic necrosis. Bernard used a mixture of bile and olive oil. Since that time, these and similar experiments have been repeated; gastric juice, duodenal contents, solutions of acids, alkalies, formalin, bile and bile salts were found to have the like effect, while less irritating substances had little or none.

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The work of Opie (1901), in which he produced acute pancreatic necrosis in animals by the injection of bile into the duct and his publication of an autopsy finding, in which a small gallstone obstructed the ampulla of Vater in a patient dying of acute pancreatic necrosis, linked up much of this experimental work with the findings of the disease in human beings. Five years later, Flexner proved that the essential constituents of the bile, necessary to cause pancreatic necrosis, were the bile salts, of which the *taurocholate* was the more active. He also showed that the mixture of mucin, due to its action as a colloid, with the injected material rendered it less active. It had been observed that the passage of a gallstone through the common duct, resulted in a dilatation or paralysis of the papilla (Vater's). This was responsible for the theory, advanced by Hess, and by Williams and Buck, that acute pancreatic necrosis was caused by a damming back of the duodenal contents into the pancreatic duct.

By his experimental work, Archibald has done much to explain an important factor in the production of the lesions of acute pancreatic necrosis. Working on cats, he found that the small sphincter at the common duct orifice, first described by Oddie (1887), furnished this link. Oddie had demonstrated that irritation of the duodenum or even stomach mucosa, either mechanically or with dilute hydrochloric acid, or stimulation of the vagus would cause spasm of the sphincter and that the sphincter, in dogs, would resist pressure of fifty millimeters of mercury. By the *introduction of infected bile* under just sufficient pressure, so as not to overcome this sphincteric action, Archibald was able to cause the death of a cat from acute pancreatic necrosis in twenty minutes. He enumerated a group of factors, the necessity of the presence of which makes understandable certain conditions in the causation of the disease which otherwise would be hard to explain. These three factors were: *first*, changes in the composition of the bile due to infection, which increases the proportion of bile salts; *second*, undue resistance, perhaps amounting even to spasm of the common duct sphincter; *third*, abnormal rise of pressure in the biliary system, either in the gall bladder or the common duct.

These experimental observations, linked up with observations on what is known of the occurrence of attacks of acute pancreatic necrosis in human beings, would seem to make a case for the usually accepted *"biliary reflux" theory* as to its etiology. The association of the attacks with gallstones and biliary infection accounts for the necessary change in the bile. The occurrence of an acute attack after a hearty meal would account for the necessary spasm of the sphincter of Oddie, as would also gastric hyperacidity or duodenal inflammation. The occasional finding of a gallstone impacted in the ampulla suggests that, in certain cases, a stone may have been impacted and then passed; this would explain the previous damming back of infected bile.

But, having enumerated these various biliary conditions, which would, apparently, be causes of the acute lesions of the pancreas, one must consider certain observations which would seem absolutely to refute the possibility of the disease being caused by a reflux of infected bile in other cases. These are, that anatomical conditions in some cases make it impossible that a reflux of bile could have been possible etiologically. Opie, in his book on diseases of the pancreas, quotes various case reports in which reflux of bile could not have been the cause of the pancreatic necrosis. In one case report by Eliot, the duct of Santorini was the larger and entered the duodenum about one and five-tenths centimeters above the papilla, through which emptied the smaller duct of Wirsung and the common duct. The necrosis, in this case, was most marked in the portion of the gland drained by the larger duct of Santorini. Johnstone reported two cases of pancreatic necrosis in which the pancreatic duct opened into the duodenum one or two centimeters above the common bile duct opening. Bassett reports one case in which the necrosis involved the area drained by the small duct of Santorini, which entered the duodenum through a small diverticulum above the papilla. It is also known that, at autopsy, the pancreas may be found to be extensively stained with bile, but exhibit no necrosis.

In these cases, reflux of bile could not have occurred. The theory that the duodenal contents might be forced back into the pancreatic duct and would cause pancreatic necrosis, would have to be the explanation of the etiological factor in these latter instances, admitting the reflux theory. Many years ago, Polya showed that duodenal contents injected into the duct would cause pancreatic necrosis. But, experimentally, this could occur only when the injection was made under pressure. Attempts to cause necrosis of the pancreas by experimental duodenal obstruction below the duct have not been successful. White and Owen have reported a case in which a carcinoma extending from the stomach, so dilated the duodenum and the sphincter of Oddie that it allowed free flow of the duodenal contents, bile and pancreatic juice into the pancreatic duct without causing any particular damage to the pancreatic tissue.

To add to the confusion of thought, the *theory of infection* of the pancreas by means of retrograde infection through the lymphatics from the gall bladder, appendix or a duodenal ulcer, has been advocated by Bartels, Arnsperger, Franke, Deaver, Pfeiffer and Sweet and must be considered. It would seem to me that the theory of infectious origin of pancreatic necrosis would appear to be contrary to the fact that, although in some cases, one finds enlarged lymph nodes about the head of the pancreas, in the series of 32 cases examined in St. Luke's Hospital only one showed

this condition. Also, the type of lesion found does not coincide with the original infectious process present elsewhere. Cultures made at the time of operation are nearly always sterile. Furthermore, when a patient recovers without operation and a residual lesion occurs, instead of presenting the usual type of abscess which one expects to find in an infectious process, the lesion occurs as a cyst or an area of fibrosis in the body of the pancreas surrounding a softened, cheese-like material which is not pus. In only one case of the group reviewed from the records of St. Luke's Hospital, was there apparently a real infectious lesion of the pancreas. This patient died from an infected, portal phlebitis and there were multiple, small abscesses in the pancreas. It seems to me worthy of note that, in considering the infectious theory in the etiology of acute pancreatic necrosis. this patient obviously had a real hematogenous infection of the pancreas which did not cause the lesion of acute pancreatic necrosis. It is difficult, therefore, to accept the theory of infection which theory rests on a retrograde lymphatic infection.

Also it seems to me that if one consider the various factors in the pathological process, it is easy to accept the explanation that the damage is caused by a reflux of some material into the duct. The necrosis in the pancreas and the hemorrhage in the gland which occur in some cases and not in others, and the varying amounts of fat necrosis about the gland, are explainable on the basis of the liberation and activation of the gland's ferments. The trypsinogen in the gland is inert until it becomes activated into trypsin. A reflux of inert substance or a moderately irritating substance which does not injure the duct wall would not cause any contact with the trypsinogen in the gland to activate it. This explains the necessity of pressure or of a substance sufficiently irritating as to injure the epithelial lining of the duct, while the pancreatic necrosis does not necessarily occur with gradual dilatation, such as reported in the case of White's and Owen's. On the contrary, if the reflux of material is sufficiently irritating to destroy or to penetrate the duct wall and enter the pancreatic body, trypsinogen is activated, necrosis occurs and the necrotic material activates more trypsinogen. The walls of the large or small blood vessels are digested and eroded, blood escapes—the calcium of which activates more trypsinogen—and further extension of the process takes place, so that, in a severe instance, the whole gland may become necrotic and destroyed.

This examination of the etiology of acute pancreatic necrosis is necessary in order to understand the pathology and the symptomatology as well as the prognosis and treatment of the condition; for this reason, it has been reviewed rather more in detail than may have seemed necessary.

PATHOLOGICAL FINDINGS

The pathological condition found at operation or at autopsy varies with the factors which etiologically have been operative. It varies from a moderate amount of thickening in the region of the head of the pancreas or edema involving more or less of the whole gland to a hard, indurated condition of the organ, which, while changed in consistency, may not be very much changed to gross appearance. Various areas, or the whole gland, may be mottled with hemorrhagic areas which are red, or necrotic areas which are green. This process may extend even further so that large areas of the gland are replaced by soft, necrotic sloughs. While it has been asserted that the damage to the gland occurs with the primary etiological factor, there can be no doubt that the extension of the process may occur from any one of the simpler conditions herein mentioned to the entire destruction of the gland. This, as has been stated before, has been demonstrated by many of the cases examined in the series from St. Luke's Hospital, where the simpler condition was found at operation and the more advanced lesion at autopsy.

Also, the pathological condition found, associated with repeated attacks of pancreatic lesions, are of interest. A patient operated upon by me for acute pancreatic necrosis, who gave a history of a milder attack which was diagnosed as gallstones a year previously, exhibited, in addition to the acute lesion in the head of his pancreas, an area in the region of the tail which was fibrosis surrounding cheese-like material which had resulted evidently from a previous limited attack of acute pancreatic necrosis. Another case from the records of St. Luke's Hospital, was that of a woman who had been operated upon for an acute attack wherein nothing was done to the pancreas; two years subsequently she showed, by X-ray examination, a calcified area of the pancreas which was obviously a walled-off old pathological lesion. The hospital records recorded similar cases. In one, at operation for acute pancreatic necrosis with removal of a microscopically normal gall bladder, the whole pancreas appeared hard with no area of softening, although there were some areas of fat necrosis. A pancreatic cyst, containing a quart of fluid developed three weeks later. Another patient, who had been operated upon for acute pancreatic necrosis in another hospital six years previously, subsequently developed three attacks two years apart, during the first and third of which a pancreatic cyst was drained.

At the time of operation for a pancreatic lesion, fat necrosis is a prominent feature. It varies in extent, and in certain cases where there is only a moderate amount of thickening in the head of the gland which is found associated with an acute gall bladder lesion, the only way in which a clinical difference between an acute and a chronic lesion of the pancreas can be made is by the presence or absence of fat necrosis. In the presence of an acute pancreatic necrosis, apparently the basement membrane of the acini, as well as the

connective tissue binding the lobules of the gland, is sufficiently destroyed to allow an escape of a certain amount of lipase, the fat-splitting ferment. This attacks the fat in small areas, splits the fat globule into fatty acid and glycerin and the fatty acid combines with calcium salts to form an insoluble soap. These areas appear in the omentum, mesentery and sub-serous fat and on the surface and about the pancreas, as small opaque white spots. It is easy to understand this direct extension of the pancreatic ferments, but I know of no adequate explanation of why these small, isolated areas of fat necrosis, so diagnostic of pancreatic involvement, occur at a considerable distance from the gland or how the lipase is carried to these distant areas. Instances of acute pancreatic necrosis have been reported in which areas of discoloration and edema have appeared in the skin about the umbilicus; and in one case in both loins, due to subcutaneous fat necrosis by direct extension. In one patient, operated upon by me, at autopsy the necrosis had extended along the retro-peritoneal fat as far as the pelvis. In the severe cases of acute pancreatic necrosis, where the pancreas has been severely damaged, the surrounding peritoneal area is involved and there is found a bloody fluid exudate in the upper abdomen or in the lesser peritoneal sac, known as the characteristic "beef broth" exudate.

SYMPTOMATOLOGY AND CLINICAL DIAGNOSIS

A consideration of the different pathological conditions which may be present at the time of operation, resulting from the various etiological factors, makes it very easily understandable why so few cases clinically are diagnosed. The symptomatology must depend on the pathological condition causing the symptoms and will vary from those of an acute fulminating attack, where the symptoms will resemble those of acute, high intestinal obstruction or a perforated gastric or duodenal ulcer, to an attack which develops in the course of an acute gall bladder infection, where the gall bladder symptoms predominate or precede the pancreatic symptoms. Again, the patient may develop a moderately acute pancreatic lesion and when a lower abdominal operation is performed, the diagnosis of acute pancreatic involvement rests only on the finding of areas of fat necrosis in the mesentery; this occurred in one of my own cases. Therefore, an attempt to formulate a symptomatology which would be diagnostic for all cases is impossible. Furthermore, in many instances the pre-laparotomy, pre-autopsy diagnosis cannot be made; indeed, the condition may not be suspected.

In the presence of an *acute* abdominal catastrophe, there are certain symptoms which aid in ruling out the probability of other lesions and make the diagnosis of pancreatic involvement probable. Frequently, one may elicit a history of previous gallstone attacks, or even mild symptoms which would make one suspect previous attacks of a mild pancreatic lesion. The disease is somewhat more apt to occur at the age and in the type of patient subject to gallstones, but a patient, aged only 24, was operated upon recently at St. Luke's Hospital, with a diagnosis of acute appendicitis. Also, I have been informed, by personal communication, of a child three years old who was operated upon after a correct diagnosis, in whom a marked pancreatic necrosis was present. It is of interest that, while operations for gallstones are performed on women compared with men in the proportion approximately of three to two, these figures are reversed with respect the incidence of pancreatic necrosis.

The *pain is acute,* boring in character, frequently radiates into the back and, in severe cases, there is marked prostration, collapse and vomiting. In these severe instances, a perforated duodenal ulcer or a high, acute obstruction well might be suspected; the only help to diagnosis lies in thorough differentiation. A perforated ulcer is associated with board-like abdominal wall rigidity and while rigidity may appear late in pancreatic necrosis, it does not occur early as in ulcer perforation. A patient with an acute pancreatic lesion writhes around in bed; when there exists ulcer perforation, usually he lies still to prevent irritation of the inflamed peritoneum. Perhaps loss of liver dullness may be demonstrated in ulcer perforation. Vomiting and inability to move the bowels may give rise to the suspicion of high obstruction. Here, the region and character of the pain, localized tenderness and, occasionally, thickening in the region of the pancreas may assist in the diagnosis. Also, while there is elevation in the leucocyte count with both ulcer perforation and acute pancreatic necrosis, there is no early leucocyte elevation in obstruction. The ordinary symptoms of pulse rate, temperature elevation, vomiting, urine examination and blood count, practically would be alike in acute pancreatic necrosis as in any other inflammatory or necrotic abdominal lesion. In cases which begin with acute, infectious biliary conditions, as a rule, the symptoms of the biliary condition will render possible some lesion of this system to be diagnosable. Radiation of the pain to the left and an increase in the severity of the symptoms may arouse suspicion of pancreatic involvement. A dusky pallor of the face, head and upper portion of the body has been described as symptomatic of the acute pancreatic lesion, but this, probably, occurs as a part of the severe shock exhibited in the fulminating cases and, as a dependable diagnostic sign, its presence or absence is of questionable value.

Laboratory aids in the diagnosis may be of value, but not so much as one would wish. A flat X-ray film may help to rule out ulcer perforation by showing the absence of free gas in the peritoneum; it may demonstrate a localized distended loop of intestine in obstruction in the acute cases. In the more slowly developing pancreatic

lesion, the presence of a mass in the normal region of the gland may be demonstrable. It was possible in one case of my own to rule out, by means of a barium *clysma*, a suspected carcinoma of the transverse colon and to demonstrate that the tumor was the pancreas. Again, occasionally an enlargement of the head of the pancreas, by a change in the contour of the duodenum, may be demonstrated in a more slowly developing lesion.

One would rather expect that, with extensive damage to the pancreas, a change in the *blood sugar values* could be shown, but this observation has not proven to be of any great value in the early diagnosis, even when there is present a marked lesion. Attention has been called to the value of the *determination of diastase* in the blood and the urine as a diagnostic aid; it is stated that while increased values may occur from other acute abdominal conditions, negative findings, provided that determinations are made between twenty-four and thirty-six hours after onset of the symptoms, exclude any pancreatic pathology.

The most commonly made clinical diagnosis is, acute cholecystitis or a common duct stone. In an article by deTakats and MacKenzie (1932) in a series reviewed by them, eight-one and two-tenths per cent of the cases revealed biliary infection as a primary cause of pancreatic pathology. Also it is of interest that Heuer, in a study published this year, found from the mortality in a large number of cases of gall bladder surgery, that forty-eight deaths were due to acute pancreatitis; this was 2 per cent of the total mortality. From Heuer's report, together with a not inconsiderable number of progressive cases following gall bladder operations in the series examined at St. Luke's Hospital, it seems to me that this is another reason for opposition to the application of an universal rule for operative delay in all acute gall bladder cases. There should also be considered in the study of the symptomatology of pancreatic disease, the evidence that patients may get over a mild attack but this may be followed by a more serious one. Furthermore, not infrequently after operations on the biliary system, patients have more or less severe attacks of epigastric pain, radiating into the left side or into the back; this can best be explained by assuming that such symptoms are caused by some form of post-operative pancreatic pathology, from which, often, they recover. It has been mentioned in discussing the question of pancreatic pathology, that acute attacks may be followed by the formation of cysts or so-called pancreatic abscesses.

THERAPEUTIC PROCEDURES

In considering the therapy of acute pancreatic lesions, there must be considered a few of the various facts and observations connected with its pathology and the cause of the affection. It is known that certain patients, if not initially too severely ill, will get well without operation. It is known that a patient with a very severe, fulminating attack will die anyway and in fact, may die on the operating table. It is known that where an operation is done and there is attempted the prevention of further reflux of bile, by means of a cholecystostomy, the condition may progress. It is further known that, where the pancreas is swollen and obviously damaged, if the posterior layer of peritoneum overlying it is split and drainage is instituted to the pancreas with the idea of allowing escape of further products of necrosis, in some cases this procedure may constitute a life-saving measure: a large part of the pancreas may slough out from the drained area. In the presence of such a lesion, assuredly, that patient would have died without an operation. In other cases, where the patient recovers with practically no drainage, one may suspect that the operative procedure had very little significance. If one accepts the theory of infection as the cause of the pancreatic damage, one's inclination would be to incise the affected area and drain it freely. While this was previously done, all the evidence now is that it has no actual value but may do harm by further injuring the gland itself and causing extensive spread of the fat and gland necrosis. This makes a definite plan of procedure suitable for every case a difficult one.

Even though it has been shown that implantation of masses of dead pancreatic tissue in the peritoneums of dogs will cause death in a comparatively short time by "intoxication", which probably is due to absorption of split protein, if a patient is in acute shock due to the pain and the severity of the toxemia from a severe lesion, immediate operation should be postponed. Such a severely shocked and poisoned patient endures anaesthesia poorly and, as before mentioned, even with a short operation, may die on the table; hence, the possibility of saving such a patient by any operative procedure is very small. If the operation temporarily is delayed and the patient dies before surgical procedures are performed, safely it may be assumed that no operation would have saved him. In some articles on the subject, the fact that more cases died following early operation than after delayed operation, this observation is advanced as an argument for delaying operation in all cases. I do not believe that this is a justifiable conclusion because it is in the severe, fulminating attacks that fatal termination would have occurred anyway and had the operation been postponed never would it have been possible to do it, inasmuch as the patient would have died before it could be performed. Therefore, accepting this premise, a very severely ill patient, in shock, should have administered to him intravenous and other therapy to lessen shock before operation. The less severely ill patient should be operated upon without delay. This is on the assumption contrary to Archibald's theory that the maximum damage has been done by the primary reflux. However, after all the theoriz-

ing, it must be recognized that a clean-cut preoperative diagnosis seldom is made.

Operative treatment is instituted with three objectives: First, to prevent further damage to the pancreas, some of which may be caused by swelling and acute edema in the gland; this is accomplished by splitting the peritoneum overlying the gland; *second*, to allow subsequent escape of necrotic material or exudate from the gland; an attempt to open into the gland tissue itself, unless there is fluid or markedly broken down, sloughy material, would only do more harm than good; this never should be done in the presence of a hard, indurated gland; drainage best is accomplished by a folded rubber dam and never by tubes; any necrotic material will find its way out through the sinus formed by the rubber dam and a tube might cause death from hemorrhage by erosion of one of the larger blood vessels in this area; this occurred in a case of my own several years ago; and *third*, the aim of an operation is to prevent further influx of infected bile into the pancreatic duct by means of drainage of the gall bladder or the common bile duct, preferably the gall bladder. If the pancreatic lesion has been caused by a reflux of bile this procedure should be of value. If, as stated earlier in this paper, this "reflux" could not have been the cause of the lesions in certain cases, it is, of course, valueless but one cannot know in the individual case operated upon just what the etiological factor has been. However, as reflux of some type or degree probably is the most common etiological factor, biliary drainage should be done. One case impressed the value of this procedure on me several years ago. A patient who was operated upon in St. Luke's Hospital by Dr. M. K. Smith and upon whom a cholecystostomy was performed, was exhibiting a favorable convalescence when suddenly she quite obviously had a second attack of pancreatic involvement. Drainage from the cholecystostomy had ceased but the symptoms disappeared on the re-establishment of this drainage.

If there are stones in the common duct, these should be removed, but this operation is not always effective, as has been proven by the progression and occurrence of further pancreatic lesions. After institution of biliary drainage, an extensive operation cannot be done when the patient is very ill. Theoretically, one should establish the fact that the common duct is patent into the duodenum, but probing of the common duct may cause swelling and edema and traumatism at the ampulla of Vater, thus further increasing the possibility of reflux of bile. It has been suggested that cholecystectomy would be the ideal procedure. *First*, by removal of the focus of infection and thus the elimination of one etiological factor, that is, a change in the bile with its increase in bile salts which occurs with infection; *second*, by causing dilatation and relaxation of the sphincter of Oddie, which occurs after cholecystectomy; however, before this dilatation and relaxation occur and unless drainage is also instituted, pressure in the common duct is increased which would more likely result in reflux of bile into the pancreatic duct if anatomical conditions were such as to allow this. Furthermore, the less there is done in these severely ill patients, the better the prospect of their recovery. It might be expected that, with the extensive damage to the pancreas, there would be more evidence of failure of its function (as shown by elevation of the blood sugar), but it is surprising in many cases how little there is of this sign. In some cases, however, there is sufficient impairment of function to make the use of insulin of considerable value in post-operative treatment. Therefore, post-operative quantitative examinations of blood sugar regularly should be made.

Recurrences of attacks, often of a severe or fatal nature, after recovery from a primary operation for acute pancreatic necrosis and where biliary drainage had been instituted, seemed to indicate that it would be good surgery to remove the gall bladder in these patients as prophylaxis against further pancreatic damage after recovery from their first attack. However, it must be remembered that not in all cases is the etiological factor biliary reflux. In one of my own patients a so-called pancreatic abscess developed two years after the gall bladder had been removed, although it is probable that the primary damage occurred at the time of the acute cholecystitis for which cholecystectomy had been done.

The title of the subject of this paper is "Diseases of the Pancreas, Especially Acute Pancreatitis and Its Treatment". I have taken so much space to the subject which was especially assigned, that it leaves little to cover other aspects of pancreatic disease which might be included under the general title. Including only those diseases which may be treated by surgery and omitting all mention of diabetes, this leaves for consideration the subjects of cysts of the pancreas, chronic pancreatitis, carcinoma of the head of the pancreas, pancreatic calculi, congenital anomalies of the pancreas, pancreatic trauma and, finally, those adenomata or other small pancreatic tumors to which, in the last few years, attention has been called as the cause of hyper-insulinemia with a resultant hypo-glycaemic state.

Cysts of the pancreas are divided into true cysts and pseudo-cysts. True cysts may be (1) congenital; (2) retention cysts due to blocking of the duct by chronic pancreatitis or calculi; (3) neoplastic in origin. These are all rare. Ecchinococcus cysts of the gland are very uncommon. Most pancreatic cysts, even though such are not common pathological lesions, are pseudo-cysts.

Korte, some twenty odd years ago, divided cysts of the pancreas (of which he had collected one hundred and seventeen cases) into (1) those of traumatic origin; (2) those due to inflammation; (3) those of unknown etiology. Of these cases, there were thirty-three in the first, thirty-

three in the second, and fifty-one in the third group.

With our present knowledge of pancreatic pathology, I believe that we are justified in assuming that, whatever may be the primary etiological factor—traumatism or primary pancreatic necrosis in the pseudo-cysts—the secondary factor is the same in all of them, namely, a breaking down of the tissue with the activation of trypsinogen and a more or less extensive destruction of pancreatic tissue. This results in the lesion of acute pancreatic necrosis. If limited in extent, it may eventuate in recovery, as must frequently happen in the mild cases. This may accompany, or may be diagnosed clinically, as acute cholecystitis. If the lesion is localized in only a portion of the pancreas and this advances to liquefaction of pancreatic tissue, a pseudo-cyst forms.

The records of a group of cases examined at St. Luke's Hospital show instances where one of these cysts may disappear spontaneously and may recur either without or after an operation. It may be encapsulated and be demonstrable in the X-ray films as a calcified area in the body of the pancreas, or may be cured by the operative procedure of drainage. Usually it is stated that cysts do not form until several months, or even longer, after traumatism or injury to the pancreas. This is not necessarily so, as was instanced in the previous consideration of the pathology of acute pancreatic necrosis where we mentioned that a large cyst formed within three weeks of a primary attack of necrosis.

Cysts of the pancreas may attain large size and be present in the epigastrium or to the right or to the left of the median line. Also they may extend behind the stomach so as to fill the space occupied by the lesser peritoneal sac. While it is true that a few of the smaller cysts may disappear spontaneously, the larger cysts must be treated by surgery. Dissection of such a cyst is a most difficult and dangerous procedure. If one is dealing with a pseudo-cyst, drainage of the sac usually will result in a cure even if a fistula persists for sometime. Where a cyst is lined with epithelium, simple drainage may not be effectual and marsupialization is the proper procedure. When pancreatic fluid drains from the cyst, means must be taken to prevent the digestion of the skin of the abdominal wall.

Chronic pancreatitis may be divided into two varieties: inter-lobular and inter-acinar. The *inter-acinar pancreatitis* is considered to be the result of arteriosclerotic changes; usually it is associated with diabetes. The *inter-lobular pancreatitis* is most frequently associated with biliary tract disease, although cases have been reported in which duodenal ulcers would seem to have been the etiological factor. This type of pancreatitis rarely is diagnosed; usually it is observed as a pathological condition in an operation for gallstones. In certain gall bladder operations, when the pancreas is palpated, often it is found to be hard and indurated, most frequently about the head, sometimes throughout its whole extent. In some cases of biliary tract disease, when the pain is epigastric and is referred to the left or into the back, probably pancreatic pathology is responsible for this symptom.

It is interesting to note, however, as has been stated in the consideration of acute pancreatic lesions, that a number of the cases where the history charts at the time of operation for some biliary tract lesion, showed that when there was a thickening or induration of the pancreas, this advanced later, to acute pancreatic necrosis. Usually, these chronic inflammatory lesions are ascribed to "secondary infection" from the biliary system, duodenal ulcer or to appendicular infection by lymphatic invasion. It is suggestive, however, that these same lesions, as far as can be made out macroscopically, may develop into acute pancreatic necrosis where all of the evidence would point to the reflux theory of etiology. Of course, as far as operative inspection is concerned, there is no way of determining whether the condition is an early, acute process or one which slowly has been developing into a chronic one from its inception.

There has been little done or even suggested to aid in the diagnosis of a chronic pancreatitis, except by operation, apart from some of the diagnostic work concerned with the examination of pancreatic ferments by means of analyses of duodenal contents obtained by the passage of a duodenal tube. In the presence of chronic pancreatic disease, a sufficient amount of pressure on the common duct, in those cases where the duct passes through the head of the pancreas, may cause obstructive jaundice. In such a case, or where the pancreas is found hard and indurated at operation, a differential diagnosis between chronic pancreatitis located in the head of the pancreas or carcinoma in the same region may be most difficult. If a diseased gall bladder also is present and the evidence is more strongly in favor of an inflammatory process than a neoplasm, the gall bladder should be removed and drainage of the common duct instituted. If there is reason to believe that a carcinoma is the more probable diagnosis, a cholecystogastrostomy or a cholecystoduodenostomy should be done.

Carcinoma is the most common neoplasm of the pancreas. It is rarely metastatic but not infrequently involves the gland by direct extension of a growth from the stomach. When primary, it occurs in the region of the head of the gland in more than 50 per cent of instances. This neoplasm is not amenable to surgical cure, although various operative procedures have been devised which deal with the common duct, implantation of the remaining gland into the intestine, etc. The danger of the operation and the poor prospect of cure at the present time, would not make operation of pancreatectomy—partial or complete—justifiable. Palliative operation,

however, is indicated, when the tumor in the head of the pancreas causes obstruction to the common bile duct with its resultant symptoms and signs.

A deep, increasing, painless jaundice associated with clay-colored stools, an advancing icteric index, loss of weight, anorexia, afebrile state, and an enlarged, palpable gall bladder, usually will serve to make the differential diagnosis from stone in the common duct, for which pancreatic neoplasm is most apt to be mistaken. There are, as in the symptomatology of most instances, exceptions which may confuse the diagnosis, but these cannot be considered here for lack of space. An important finding is that of the constant presence of blood in the duodenal drainage, associated with failure to recover gall bladder bile.

Operation, however, should always be done for the purpose not only of confirming the diagnosis but also to relieve the biliary duct obstruction with its interference with digestion, severe itching of the skin accompanying the deep jaundice and the damage to the liver with associated interference with all of its functions due to back pressure of the bile. If operation is delayed until extensive liver damage has occurred, the operative danger is increased and the prognosis grave.

An anastomosis between the gall bladder and duodenum or the stomach by the suture method, under local infiltration anaesthesia, will relieve the jaundice, stop the itching and prolong life for several months, if done before too much injury to the hepatic parenchyma has resulted. Of course this operation does not relieve the obstruction to the escape of pancreatic ferments into the intestine. As the carcinoma increases in size there will be increasing pain, but, all considered, the operation is worth while. Occasionally a patient may live for many years after such an operation and here it must be assumed that probably the diagnosis was in error and that the symptoms had been caused by a chronic pancreatitis instead of by a carcinoma.

Congenital anomalies of the pancreas have little medical significance but some, although rare, have a limited surgical importance. They may be explained on the basis of abnormal embryological development of the *anlagen* from which the gland develops. The most common anomaly is accessory areas of pancreatic tissue which on occasion may be found in the walls of the upper gastrointestinal tract.

Annular pancreas is a rare developmental anomaly. In 1929, Brines (*Annals of Surgery*, 1929, Vol. XCII, p. 241) stated that only twenty-nine cases had been reported. In this condition, the duodenum passes through a ring of pancreatic tissue instead of lying to the right of the gland. It is curious that while this condition is so rare, that two instances, which have not been reported, were observed at operation at St. Luke's Hospital in the last seventeen years. In one, operated upon by Dr. F. S. Mathews, the anomaly had caused a duodenal obstruction for which gastroenterostomy was done. In the second case (one of my own), accompanied by a cholecystitis, swelling of the gland caused by biliary obstruction (for which cholecystectomy with biliary drainage was done), there has been no recurrence of symptoms in the past five years.

Pancreatic calculi are uncommon; a diagnosis during life is rare. Most cases are reported from autopsies. Usually, stones are small and multiple and most often reported as the size of a pea or a bean, although they may be as small as a grain of sand; one is reported which measured about two and a half inches in length and one-half inch in diameter. The main constituent of pancreatic stones is calcium salts. They are more likely to be found in the head of the pancreas where the ducts are larger but may be located anywhere in the gland. They occur most frequently in males.

The symptoms may be due to the presence of stones in the duct; then they may produce pain; or, due to the various changes which occur in the pancreas as a consequence of their presence (such as impairment of the function of the gland dependent upon changes in its parenchyma or to blocking of the duct with formation of a cyst). The stone may become impacted in the papilla of Vater and thus cause jaundice if they block the common bile duct at its point of emptying into the duodenum. If the stones are large and contain a sufficient amount of calcium salts, they should be demonstrable in an X-ray film.

Operations for a stone in the pancreas rarely are attempted as there are no positive diagnostic signs except by X-ray diagnosis, and, judging from autopsy reports, probably these stones exist in a large number of cases with no more symptoms than come from so-called "silent" gall stones. They are more apt to be discovered in an upper abdominal operation. If pancreatic calculi have come close to the surface and caused a cyst or an area of local softening, they should be removed. Cases have been reported where they have been removed through an opening in the duodenum by extraction from the ampulla of Vater. Probably, in nearly all of these cases, it was believed that the stone causing the obstruction was an impacted gall stone. As before stated, the condition is so rare and has such uncommon surgical significance that it is unnecessary to go into further detail here.

Wounds of the pancreas occur as penetrating wounds, gunshot wounds and subcutaneous rupture. In any one of these types, while the pancreas may be the only organ injured, nearly always there is more or less severe injury to the other viscera which is severe enough to attract immediate attention and operation. Here we have not space to elaborate the symptomatology. It must suffice to call attention to the fact that a sufficiently severe injury to the pancreas will cause death by pancreatic "poisoning" due to self-destruction of the pancreatic tissue, unless drainage promptly is instituted. In suspected subcu-

taneous injury, an increase of the diastase in the blood or the urine may aid in the diagnosis. If the injury is not sufficiently severe to cause death, a pseudo-cyst later may occur. In all upper abdominal injuries, whether other viscera are or are not injured, the possibility of pancreatic damage must be borne in mind.

Within the last few years, the condition of *hypoglycaemia*, which is ascribed to hyperinsulinism, has attained considerable prominence in the literature. Apparently the affection is a recognizable clinical syndrome (as given by Seale Harris and Holman and Railsback) characterized by symptoms of weakness verging on exhaustion, nervous irritability, easy fatigability and extreme hunger; in the more severe cases there occur muscular twitchings and tremor, impairment of vision, diplopia, unsteadiness of gait, excessive perspiration, loss of emotional control. In the most advanced instances, there are mental confusion, disorientation and even epileptiform attacks, convulsive seizures, syncope, semi-stuporous attacks, coma and finally death. Early in the disease, the symptoms usually appear before meals or in the early morning before arising and are associated with weakness and an extreme feeling of hunger. The symptoms are relieved or ameliorated by the taking of food, especially foods containing sugar. The blood sugar is found to be exceedingly low and, as the condition progresses, may be below 30 mgm. during the severe attacks.

Pathologically, in a certain number of instances, these symptoms are associated with tumors in the pancreas. These tumors are adenomata or carcinomata; they may be situated where they can be seen, presenting on the surface of the gland at operation or may be buried in the gland-substance where they cannot be found at operation. It is difficult to understand, knowing there are more islets in the pancreas than are necessary to produce an adequate amount of insulin, why a small tumor only a centimeter in diameter may produce these symptoms of hyperinsulinemia. Microscopical examination shows that in the tumors these cells resemble islet cells, that they are hyperactive and apparently produce an abnormal amount of insulin.

The first successful operation for cure of the hyperinsulinism by removal of such a tumor was done in 1929. In April, 1933, Graham and Womack (*Surgery, Gynecology and Obstetrics*, Vol. LVI, p. 728) reported seven cases of successful removal of islet tumor with relief of symptoms and no reported mortality. Unfortunately, recognition of the clinical syndrome does not always insure the finding of a tumor of the pancreas and the cure of the disease by removal of such a tumor. Graham reports one case in which a tumor was found and removed with improvement of the symptoms, only to have the symptoms recur and at reoperation a second tumor was found and removed. Disease of the adrenal glands, certain pituitary tumors, primary carcinoma of the liver, injury to the liver function by neonarsphenamine —or by phosphorous poisoning—and scleraderma may be associated with hypoglycaemia. Apparently certain conditions in the pancreas itself may present the same hypoglycaemic symptoms which have been treated by removal of a large part of the gland. In general, the operative results of these latter cases have seen somewhat disappointing, although some improvement has been reported; it may be that the failure of improvement is due to an overlooked adenoma in a portion of the gland which is allowed to remain.

The striking improvement, however, in the case where a tumor is found at operation and can be successfully removed, makes it worth while for everyone to have this etiological factor in mind as, by operation, if the tumor can be found and successfully removed, the patient can be cured, whereas, otherwise, the affection would progress to a fatal termination.

ABSTRACTS

BEST, R. RUSSELL.

Abdominal Incision in Lesions of the Rectum Rectosigmoid as Related to the Colostomy. S., G. and O., Vol. LIX, No. 2, August, 1934.

The author states that in the consideration of abdominal incisions as related to the colostomy two essentials are demanded: first, a correctly placed incision ample enough to carry out thorough exploration, and any necessary intra-abdominal procedure. The carrying out of a properly placed colostomy, either loop or end type, and either temporary or permanent. Those essentials are embodied in the paramedian incision in the author's opinion. By using that incision closure can be made by suturing muscle to muscle, and fascia to fascia; any colostomy will be completely surrounded by muscle. In the author's technique continuous chromic suturing is used in the peritoneum, while interrupted sutures of chromic are used in the fascia; the skin is closed with interrupted dermo sutures. An end or loop type of colostomy may be made in this incision. If the end type is used, the peritoneum should be brought snugly about the end of the protruding viscus. In the author's experience this incision heals in spite of the constant contact with feces. In opening the left rectus incision for the second stage operation infection is quite rare if proper preoperative management, and colon surgery technique, have been carried out.

If a temporary type of colostomy is to be made, the author, after bringing the loop of sigmoid out over a glass rod, grasps a spindle-shaped portion of the exposed bowel wall with a curved clamp, and cuts it away with the cautery. The clamp is left in place. In that way the patient is spared the unpleasantness of smelling the burning flesh when a later opening is made.

If the case of carcinoma of the rectum is operable,

the method of Lahey is followed in some cases. By separating the mesentery from the bowel wall for a sufficient length, the permanent colostomy may be made in the upper end of the incision instead of in a left McBurney incision as is done in the method of Lahey.

In any case immediate drainage of the bowel may be accomplished by means of a catheter inserted through a purse-string suture.

The author concludes that with this time-honored incision both emergency and selective operations are adequately handled, and desirable types of colostomies may be placed in both operable and inoperable cases. In no case is it necessary to use the cautery after the patient has left the operating room.

Five figures showing the incision, and the colostomy opening in the various conditions, accompany the article.

Nelson M. Percy, Chicago, Illinois.

GRAHAM, EVARTS A., AND MACKEY, W. ARTHUR.

A Consideration of the Stoneless Gall Bladder. J. A. M. A., 103:1497, November 17, 1934.

It is known that surgical results in the stoneless gall bladder are not so satisfactory as are those in which gall stones are present. The more severe the symptoms before the operation, the more complete the relief after operation seems to be the rule. The best results have been obtained in those cases who have experienced repeated attacks of biliary colic. The patients with comparatively mild symptoms have received little benefit following operation.

An analysis is given of 161 patients who were operated on for ball bladder disease, 17 of whom had stones. The ultimate results in those cases in which no stones were present showed only 60 per cent who consider themselves well. Of these cases, only 33 per cent gave a history of biliary colic, but 76 per cent of these patients considered themselves well or improved, after the operation had been performed. Moreover 82 per cent of the patients with stone gave a history of biliary colic and all were relieved post-operatively.

The presence of stone and a history of typical biliary colic greatly increases the chances for satisfactory results after cholecystectomy.

Francis D. Murphy, Milwaukee, Wisconsin.

GUIDO, FRANK R.

Intestinal Fistulas. J. A. M. A., 102:2176, June 30, 1934.

Spontaneous or post-operative intestinal fistulae are difficult problems for the physician as well as for the patient. The loss of intestinal juices causes marked changes in the blood chemistry. The toxemia resulting from the loss of these juices is similar to that which occurs in high intestinal obstruction, characterized by high concentration of urea, decrease in blood chlorides and alkalosis.

The second great difficulty in these cases is due to the fact that the pancreatic juice is a powerful digestant of tissue and rapidly digests the abdominal wall causing a slough and infection.

The author re-emphasizes a form of treatment for the intestinal fistula which he has found useful. The treatment is as follows:

Tenth normal hydrochloric acid is used to neutralize the alkalinity of the pancreatic juice thus preventing tryptic activity which is the agent particularly responsible for the destructive action to the abdominal wall in these cases. The hydrochloric acid is used as a wet dressing around the wound and a plug of gauze saturated with the acid is put into the fistula opening. An attempt is made dietetically to obtain a more solid type of fecal content. Fluid intake is limited to 1,000 c.c. a day. The author cites a case treated very successfully by this method.

Francis D. Murphy, Milwaukee, Wisconsin.

STRAUSS, MAURICE B.

The Role of the Gastro-Intestinal Tract in Conditioning Deficiency Disease. J. A. M. A., 103:1, July 7, 1934.

The fact that an inadequate diet may lead to a deficiency disease is well known; that deficiency disease may develop in man in the presence of an adequate diet because of some gastro-intestinal disturbance is not so well known.

Disturbances of the gastro-intestinal tract may lead to pernicious anemia, pellagra, "alcoholic" and pregnancy neuritis, idiopathic hypochromic anemia, and similar conditions.

Castle has demonstrated that there is a gastric defect in pernicious anemia. However, pernicious anemia could be developed as a result of a diet deficient in "extrinsic factor". Certain cases of sprue and pernicious anemia of pregnancy seem to fall into this type.

However, even in the presence of an adequate diet and a normal gastric secretion, anemia is possible as a result of failure of absorption from the intestinal tract. The author cites cases of such type from the literature and mentions one of his own in a boy of eight in whom pernicious anemia developed following two operations for intestinal obstruction following appendectomy and a second case in a man who had multiple intestinal anastomies.

Pellagra may result from a moderately faulty diet, particularly in alcoholics. The author mentions many diseases of the gastro-intestinal tract which have given rise to pellagra. The author's own cases have followed ulcerative colitis, carcinoma of the stomach, duodenal ulcer, diaphragmatic hernia, and stenosis of the small intestine. The author stresses that in most of these cases the gastro-intestinal lesion has prevented the patient from partaking of an adequate diet.

Alcoholic neuritis occurs in individuals not only because of partial inadequacy of the diet taken but in addition the anorexia and vomiting that develops further destroys the value of the diet taken.

In pregnancy neuritis, the condition generally occurs in those cases in which there has been vomiting of pregnancy thus militating against the absorption of what otherwise might have been an adequate diet.

Alcoholic and pregnancy neuritis have responded well to adequate Vitamin B diets. Both of these conditions have been shown to result from anorexia, vomiting and failure to utilization of food taken.

The author concludes that pernicious and related macrocytic anemias, pellagra, "alcoholic" and pregnancy neuritis in the temperate zone are more frequently caused by disturbances in the gastro-intestinal tract than by inadequate diets.

Francis D. Murphy, Milwaukee, Wisconsin.

SECTION VII—*Surgery of the Lower Colon and the Rectum*

Malignancies of the Colon with Especial Reference to those of the Rectal Zone*

By

JOHN F. ERDMANN, M.D., F.A.C.S.
NEW YORK, NEW YORK

IN SEVERAL previous communications on this subject I reported a series of 439 operated patients, calling attention to the relative frequencies of these growths in the recto-sigmoid, the caecum and ascending colon, the hepatic and transverse colon, the splenic and descending colon. I am, in this communication, reporting an additional 92 cases coming under my operative care during the past two and one-half years. I am satisfied, and have been so teaching for several years, that our classification of these tumors as to region should not include the recto-sigmoid as taking in the true rectum but that all growths below the junction of the recto-sigmoid should be known as the *recto-anal,* or *the rectal* and *the anal.* My object in this classification is more than two-fold as, primarily, in the rectal and anal tumors the operation is or should be a perineal one and, secondly, the results of the perineal operation in the true *rectal* or *rectal and anal* are far ahead as to recovery of those in the so-called recto-sigmoid inclusion. Granted that a perineal anus has for years been abhorred by surgeons, I wish emphatically to remark that from what I observe in the patients on whom a perineal operation has been performed by me, I would personally prefer a perineal operation with its low mortality, its post-operative functions and its ease of attention, to that of a sigmoidostomy.

When the growth involves the recto-sigmoid junction, the term in itself implies an invasion of the lower sigmoid and the proximal rectum. Any operation for a growth in this region is the most difficult to entertain and the most extensive, with a permanent colostomy as a finality and a relatively high mortality as compared with the rectal and recto-anal operations when done from below.

As a whole, I am accepting more and more patients today whom years ago I would have refused for anything but a colostomy. This is, I am quite sure, due to more adeptness and proficiency in operating and a more balanced operative judgment. In other words, patients whom I would not have accepted earlier in my career I am operating for the past ten or twelve years with a very good outlook.

Incidence and Location: Malignancies of the large intestine far exceed those of the stomach, while malignancies of the small intestine have been found by me but twice in ten years. These two instances were both of the small gut in the neighborhood of the ligament of Trietz. As my list of operations on the large gut now stands, the frequency as to location is much the same as in the former communications. In the original classification as to location, including in the former articles the rectal and recto-sigmoidal as one area, this zone was the first with the sigmoid second. As I now classify the areas, since 1928 and through June, 1934, there were 53 rectal, 44 recto-sigmoidal, 64 sigmoidal, 18 caecal and ascending colon, 18 hepatic flexure and proximal transverse colon and 19 splenic and descending colon.

The *age and sex* of the patients were rather equally divided with the growth above the sigmoid. A marked difference in sex preponderance occurs in the female in the lowest segment, i. e., the rectal or recto-anal. Out of 53 with sex noted 28 were female and 25 were male. Four of these had artificial ani only. The average age was 49, the youngest being a female of 22 and the oldest a male of 89.

The rapidity of growth in these patients is influenced as in cancer in other regions of the body by the age of the patient and the type of cell. The structures invaded primarily are mucous membrane and musculature. The more youthful the patient the more rapid the growth. The lapse of time between the initial onset of the growth and the time of operation cannot be estimated, as all calculations must be based upon and reckoned from the appearance of the first symptoms, either subjective or objective, and unfortunately often the first evidence is objective, such as mucus or blood in the stool.

Multiple growths have been encountered by me numbers of times. On one occasion, a male, 32, operated for a so-called chronic appendix, came to me eighteen months later with the same evidence

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of right lower quadrant distress as he had had before the appendectomy. Added to those symptoms were loss in weight and strength and the presence of a lump under his operative scar. A wide resection was made. Twelve inches of the ileum, the caecum, ascending colon and over one-half of the transverse colon were removed with an end-to-side anastomosis. The gut, upon examination at the conclusion of the operation, presented a definite tumor in the resected transverse colon, that was triangular in shape, about one and three-quarters inches in its base and non-ulcerated, in addition to a large foul ulcerating growth of the caecum. Several patients have had secondary operations for tumor of the large bowel years following the primary resection. It is interesting to note that the majority occurred in caecal growths, perhaps by implantation. An interesting instance occurred in the series reported by me in 1922 that may be considered a multiple growth or again may be classed as a remote appearing secondary growth. This patient had a typical Friedreich operation by me, for a large caecal growth involving the appendix, about three years before, followed by a sigmoid growth that we suspected at the end of two and one-third years. It may well be speculated that this patient had the sigmoid growth at the time of his earlier operation or that he had an implantation or a metastatic growth in the sigmoid. This latter I would consider rather unusual. This patient also belongs to the class of patients from whom the appendix is removed for the pain and distress due to back pressure as a result of an obstructing growth in the caecum or any part of the colon distal to the caecum.

SYMPTOMS

From the viewpoint of regional classification, the symptoms should vary somewhat, but in the main they are prone to slight variation. It is a well-observed fact that in growths involving the caecum and ileo-caecal regions obstruction is rare. This is due to the liquid state of the contents of the small intestine and due to the fact that these growths rarely invade the caecum in the same circular manner as they invade the colon. No acute *ileus* was observed in any of the patients in this series involving the caecum but in several instances definite colics were located in the lower right quadrant, showing in these patients upon operation a very small opening at the ileo-caecal valve, due to the growth invasion almost closing the opening of the valve. The growth invasions of the colon beyond the caecum, particularly from the hepatic flexure down, as a rule are of the annular variety and may be, and often are, accompanied by cramps, etc.; as the colonic stream thickens from absorption of its fluids just that soon will early evidence of obstruction be observed.

There is an ever-present *anaemia* in these growths and most profound when in the caecum, diminishing as the growths are found more distal, so that it is rare to find a marked secondary anaemia in the sigmoid growths, but more than likely to be markedly evident in the caecal. *Loss of weight* is present and greater, as a rule, in the caecal than the other growths; glandular secondaries less in the caecal than in the recto-sigmoid; hepatic metastases plus in the sigmoid and least in the caecal. Evident *tumor* on palpation is most easily found in the caecal growth, with the sigmoid next and then the ascending colons.

The *X-ray* is our greatest help above the proctoscope and finger reach.

The type of growth which is likely to be overlooked or questioned by X-ray findings is the growth not sufficiently advanced to become obstructive, but as a rule some contour deficiency shows, especially in several series of plates.

Some of the patients complain of a sense of distress and soreness with pressure over the site of the caecum and appendix, particularly so if the growth becomes obstructive. On various occasions I have operated upon patients for these growths who have previously been operated upon for a so-called "chronic appendix". I plead guilty to the same operative error on two occasions years ago and one recently. Our error is readily explained—recalling that an obstruction, either partial or complete, exists distal to the caecum, that the small intestine is pouring fluid contents into the caecum with the formation of a by-product of gas due to fermentation, etc., and that the egress is obstructed. The resulting dilatation of the caecum, appendix and upper colon becomes a source of pain or distress and unless great care is observed by the eye and palpating fingers the true source of the symptom is overlooked.

My first offense, about thirty-three years ago, was in a young man of 34, with a colloid carcinoma of the transverse colon. I removed the appendix (for pain in the right lower quadrant) that contained foreign bodies, was eight inches long and one-half an inch in diameter in the greater portion of its length; the caecum was not dilated enough to call attention to the importance of further search; followed in ten days by total obstruction, which I thought at this time to be an ordinary surgical complicating sequence such as obstruction by adhesions or bands. Upon opening the abdomen a growth was found in the mid-transverse colon. Recovery followed proper repair, the patient living eleven years and dying of a large growth of the right shoulder which X-ray showed to be osteo-sarcoma. No biopsy or autopsy was done.

The second of my own was in a patient who bled from his bowel about six weeks after his discharge from the hospital following an appendectomy. X-ray on this patient before operation was reported negative. Subsequent to his bleeding the X-ray reported growth in the splenic flexure.

The third (a female) occurred in my practice

this year. The patient was 52 years old and complained, when she first consulted me, of some pain in her right side in the gall-bladder zone. I tried to obtain in all ways, except X-ray and proctoscopy, a history pointing to a malignancy or obstruction. She was operated upon by me for her gall bladder and appendix, both of which were found to be diseased. About three months after the operation she returned with a frank history of blood and mucus in the stools. Proctoscopy revealed a definite carcinoma of the recto-sigmoid. This was successfully removed and the patient is now well on the way to recovery with a permanent artificial anus, a total removal of the sigmoid and rectum having been done.

Thus, again, we observe that the utmost searching examinations must be made to overcome the possibility of a mistaken diagnosis with a relatively useless operation.

A rather interesting incident occurred during August of this year (1934). A young woman, 38 years of age, from whom I removed a polyp the size of a lemon some years ago, came with a history of bleeding profusely and irregularly from the vagina. Examination revealed a multiple fibroid uterus about three and one-half months' pregnancy size, a cyst of the right ovary about the size of a grapefruit and a cyst of the left ovary about one-third that size. A sub-total hysterectomy was done. Just before I began to clean up for a closure of the abdomen a lump was found under the omentum that felt like a sponge. Upon lifting the omentum the lump was found to be a carcinoma of the sigmoid, involving slightly more than one-half the calibre. The abdomen was closed in the hope that no obstruction would occur with a proper healing time for the hysterectomy and in the meantime consent would be obtained to re-open the abdomen for work on the sigmoid. Upon questioning the patient since her operation no information has been obtained which would point to a neoplasm.

I am not inclined to lay great stress on alternating diarrhoea and constipation as by the time these occur the diagnosis by other and earlier symptoms should have been made.

Colic in the caecal area is in evidence only when the growth is sufficiently occlusive to obstruct free flow through the ileo-caecal valve or through the caput into the colon. As the disease progresses, when located in the distal colon, cramp and colics are in evidence in direct relationship to the amount of obstruction in existence. This symptom essentially is not due only to the invasion of the gut but to the consistency of the contents. As the contents become more and more firm as the terminal colon is reached, it is quite evident that the mass becomes more obstructive and a calibre in the upper colon would transmit much that, due to absorption of fluids as it migrates to the distal colon, would readily obstruct the same calibre in the distal colon. It is, therefore, safe to state that the more liquid the colon content the less appearance of colics; and the reverse, the more solid the moving mass the more evidence of colics and the earlier the obstruction.

Early toxemias are more often seen in obstructions of the proximal portion of the large bowel than in the distal half, easily explained by bacterial growth and absorption of toxins by the small intestines, by the caecal sewer trap one sees in practically all of this type and by the large areas of foul ulcerating growth present. Borborygmus may be present or absent; if present, it is likely to be of a metallic, hissing sound like that due to gas or fluid passing through a small calibre. In obstruction, partial or complete, I have called attention for years to a *metallic tinkle* heard with the ear over the caecal region when the opposite side is sharply pushed toward the median line. This sound is due to a collection of fluid contents in the caecum with gas above it. I consider this sign an infallible one of obstruction, complete or partial. In the post-operative obstructions one hears this same sound also in the small intestines and there the sign is just as infallible. The conveyance of a heart sound in ordinary obstruction is not, as a rule, so evident in these cases unless the obstruction is of long duration. When this sign (the metallic tinkle) is evident, operation should not be delayed. Fortunately for all, obstruction of the large intestine is never accompanied by the profound and grave toxic manifestations seen in obstruction of the smaller intestines.

The pains observed by these patients, excluding those of colics and spasms, in the sciatic, the lower back, perineum, etc., are due to nerve involvements and pressure upon contiguous nerves and bones by growths involving the lower sigmoid, the recto-sigmoid and the recto-anal. Pains in the lower back, sense of unfinished defecation and tenesmus all demand an examination for growth in the lower sigmoid and rectum. It is rare to have these in high sigmoid involvement. Blood and mucus in the stools, frequent trips to the toilet, loss of ambition, pallor and loss of weight are added symptoms and signs of great import. In the sphincteric area, and just above it, we may observe a sphincter failure due to infiltration of the muscle preventing the sphincteric action. I do not consider "ribbon stools" diagnostic, except in cases where the lower rectum and sphincter are involved.

The occurrence of *perforation* is not to be underrated but when there is a sharp pain in the left lower quadrant without emaciation, without anaemia, with no history of bloody or mucus stools, a patient robust, squattily built and about 45 to 55 years of age, diverticulitis should demand the first attention. There have been about twenty perforations in this series of malignant cases, all being found in the sigmoid growths with the exception of one recently in the ascending colon.

AIDS IN DIAGNOSIS

Aids in diagnosis that are of inestimable value are the proctoscope and the X-ray. No patient who has pain in the lower back, perineal or sciatic distribution, who complains of distressing flatulence, tenesmus or blood or mucus in the stool should be allowed to leave the physician's observation before a proctoscopic examination is made. No patient with abdominal colics, a sense of distress at any of the colonic flexures or throughout its course who has slowly been losing weight, with or without evidence in the faeces, should be dismissed from observation until a careful series of X-ray plates is taken. These should be taken both from a barium intake by mouth and by enema. When one suspects a malignancy or other variety of obstruction impending, it is advisable to take X-rays first by means of an enema. On several occasions we have seen acute obstruction instituted by the intake by mouth due to the formation of a rock-like mass by the barium which causes a plug at the contracted lumen and, thereby, necessitates an emergency operation.

I am disinclined to give radium and X-ray any consideration therapeutically except in the positively inoperable variety, as my experience with these agents in these growths is not pleasing.

Surgery, as early as possible, will give as good results in the colon as elsewhere. Late surgery is alleviating in the majority.

PRE-OPERATIVE TREATMENT

Thorough intestinal cleaning should be done when possible by cathartics, intestinal antiseptics and colonic irrigations; when not possible, and this type is seen too frequently, an artificial opening (decompression) should be made, with thorough cleansing by irrigations for a week or ten days before the radical operation is done.

The temporary artificial anus site is a matter of choice to the operator, but for years my selection has been the caecum in preference to the other segments of the colon, as in all growths distal to the caecum this position of the artificial anus is remote from the field of the final operation and does not interfere by newly-formed adhesions nor by soiling; and, finally, it is easy to close after its function has been terminated. The cleansing of the distal bowel through a caecostomy is readily performed by irrigation after the caecostomy is old enough—twelve to twenty-four hours—to prevent leakage into the peritoneal cavity. It is gratifying to observe with what facility the rectal tube may be introduced into the colon through the caecostomy wound during the period of irrigation. A reverse peristalsis takes place readily during this period. During the time of the functionating artificial anus and before the radical operation is performed, careful attention must be given to renal functioning and nutrition. When possible a mushroom catheter or Paul's tube is used for a few days. Such a procedure prevents the profuse liquid soiling that occurs in the early days if a tube is not used and, too, an irrigation may be carried out before the patient leaves the operating table.

RADICAL PROCEDURE

Under the heading of radical procedure one must consider the formation of a permanent artificial anus and the removal of the growth, with repair of the divided ends of the gut. Artificial anus as a temporary expedient has already been discussed but as a permanent objective several important pathological features must be considered. A permanent artificial anus is to be made only in those patients in whom we find the growth so firmly fixed to surrounding structures that removal would end disastrously or in patients in whom the contiguous and remote metastases are so extensive as to predicate an early demise with or without operative procedure. In this latter type with remote metastases, as in the liver, I have been doing the radical resection with anastomosis because a permanent artificial anus does not cause the metastases to subside and because patients with an artificial anus in this variety of pathology, living for a period of from a few months to the best part of two to three years with all the disagreeable associations of an artificial anus, could have had all the discomforts allayed or abolished by an additional risk of a small percentage.

In the permanent artificial anus patients two methods of procedure as to the growth are to be followed. In the first instance the growth is allowed to remain while in the second the growth is removed with all the surrounding tissue. The growth is left in those cases in which we find the infiltration extending beyond the possibility of total removal. Therefore, rather than excite a mushroom activity, the distal segment after the proper preparation is dropped into the abdomen and the proximal end is sewed into the abdominal wall; or, as in the lower sigmoid growths, one may leave the double-barrelled anus so that radium, if one wishes, may be applied directly from above and below through the upper and lower stomas of the bowel. In the event that the growth is removable (this applies, of course, to the lowest segment), the lower portion is liberated from the sacral groove; then a perineal approach is made to remove this portion and the whole segment with the growth is delivered through the perineal incision.

In the event of a non-removable growth in portions of the colon proximal to the sigmoid-rectal zone, short circuiting by means of a colonic or ileal by-way is in order. This prevents an early total obstruction or a series of periods of partial obstruction.

METHODS OF ANASTOMOSIS

As to the question of the method of anastomosis, end-to-end, side-to-side or end-to-side, by suture or mechanical appliance, one must judge his

own capacity for the type that he will select. The advance in ability to suture without leakage in the great majority of instances, the ability to do fairly rapid work, and the improved qualities of catgut now on the market place the Murphy button in the discard.

I have been doing the majority of my anastomoses during the past few years by the end-to-end method, doing a plastic on the small calibre and to meet with the larger end, as in the Friedreich operation, except in those instances where the gut is friable from oedema or much fat is encountered in the meso-colon. In these a side-to-side anastomosis is, as a rule, preferred. Nor do I fear the hypothetical pocketing in doing a side-to-side anastomosis, because I always make the opening extend to within one-half inch of the inverted ends.

For the past few years I am inclined in the recto-sigmoid operations to the making of a permanent sigmoidostomy and either resecting the lower gut or turning in the lower stump after one of the many excellent methods in vogue. The Coffey, Lahey and allied operations are readily performed with very satisfactory outlook.

The operation of Mikulicz is quite applicable to the growths from the hepatic flexure to the lower sigmoid. While its hospital time is longer by 25 to 33 per cent, the mortality is so much less that one should practice this type more in the sigmoid bowel than any other type of operation. Implantation, metastasis, etc., in this operation should be negligible with wide removal. End-to-end anastomosis is a safe procedure from the caecum to the mid-transverse colon as the leakage is less, but when one approaches that portion of the gut with a wide base to its mesentery attachments, either the side-to-side or the Mikulicz operation should be done. Side-to-side operations, or end-to-side, are rarely accompanied by pouching and retention if the anastomosis is so made that a pouch does not exist at the time of the operation.

The extensive operation of Miles I cannot, at present, feel is called for, particularly after closely analyzing his immediate and remote mortality.

It is customary to have an artificial anus established for seven to fifteen days before doing the radical operation. This procedure is the cause of the disappearance of the toxemias existing at the time the patient first comes under observation and permits of cleansing the bowel to the site of the growth, thereby facilitating the resection and preventing infection to a great degree. It also brings about the subsidence of the oedema often seen in the proximal portions and the subsidence of the marked distension, thereby bringing about a more normal diameter of the proximal end for anastomosis with the distal end. Finally, it is a safety vent during the repair of the suture line of anastomosis, preventing distension with gas and faeces and taking the weight off the column of faeces from the site of anastomosis, again preventing leakage to a great degree.

A very excellent device for anastomosis by the end-to-end method in the lower segment is the Balfour tube method, with invagination of the anastomosis ring; this tube acts as a by-way for both gas and faeces.

I am not strongly inclined to believe that a complete circle of peritoneum is necessary for prompt union, although I admit its usefulness in promoting repair, but I believe that in anastomosing, say the sigmoido-rectal zone or sigmoid, the first essentials are the preservation of the muscular and mucous membrane circulation, the exclusion of all fat lobules and the accurate approximation of the muscular and mucous coats.

Admitted that anastomosis in these zones is particularly prone to faecal fistula formation, then the most important step is the institution of proper and competent drainage for a few days. In the anastomosis proximal to the sigmoido-rectal zone I prefer no drain except in the skin wound.

The absence of early secondaries in the lower rectal and anal types is readily explained by the lymphatic distribution. I am also pleased by the good control many of the patients have, aided by scar tissue and proper diet.

CANCER OF THE RECTUM

The rectum is that portion of the large gut that lies retro-peritoneal and begins about the third sacral vertebra, lying in the groove of the sacrum, well imbedded in fat posteriorly and laterally, and extends to the sphincters and the anus.

It is regretted, for more accurate statistics, that a large number of operators do not make a specific classification of rectal cancer but include them all under the recto-sigmoid group. Therefore, this article is based upon my individual work.

The structure immediately above the rectal region is classified as the recto-sigmoid junction and at this point, in my experience, I have found the most frequent site of the malignancies of the colon and also the most difficult site for consideration as to the type of operation.

It is interesting at this point to call attention to the question of statistics. In an article in the September, 1930, "*Annals of Surgery*", page 434, McWhorter and Cloud report 13,500 autopsies in twenty-three years' service in the morgue at Bellevue Hospital. Of these 13,500 autopsies, for all classes of disease, there were twenty-six malignancies of the rectum, the average age being 56. Of the twenty-six there were twenty-one males and five females. Whereas, in my service, the female has been found to bear these growths in this zone more frequently than the male, having had twenty-eight in the female in a period of five and one-half years and twenty-three in the male, with unclassified sex in two. It is rather remarkable that the growths in the female were

discovered earlier than in the male. The major portion in the female were easily removed by the perineal method or route, while in the majority of males the growth was inoperable from the removal standpoint.

One artificial anus has been made in the females, while numbers were made in the males because of involvement of the prostate, base of the bladder and marked invasion through the rectal wall. Business care, absence of carcinoma terrors seen so much in women and indifference to slight morbidity may account, in part, for the late observation in the male.

The most frequent and, I might say, the usual site of the growth is in the lower segment, i. e., that portion immediately above the internal sphincter and is rare in the mid or upper portions of the ampulla. The signs and symptoms do not show early except when sufficient destruction of the mucous membrane occurs to allow of bleeding from the ulcerated area.

Bleeding is one of the early evidences, but is so frequently assigned to hemorrhoids that it is neglected as a possible sign. Then, again, we as a profession are at fault in many instances by failing to inspect and examine with the finger and proctoscope to find the cause.

Mucus discharge is also to be considered as a sign in this disease but is not present to the degree seen in the recto-sigmoid lesions.

Pain as a symptom does not appear until the superficial coats are destroyed so as to expose the terminal nerve filaments to irritation or by pressure on the nerves by infiltration. The pain is described as being more in the terminal rectum or sphincter area. Low backache is infrequent as compared to the pain of the recto-sigmoid growths. Tenesmus, frequency of desire and unsatisfied movements as symptoms are more frequent than in growths in the recto-sigmoid. Loss in weight, anaemia, etc., are slight if present at all, until the growth becomes practically inoperable. As the growth advances it may involve the sphincters to such a degree as to cause loss of control, this being due to infiltration in the tissues destroying the contractile and distensile qualities of the sphincters. Encroachment upon the prostate and bladder often creates a dysuria and frequency. In the female the posterior wall of the vagina is frequently involved and requires plastic repair after resection of the growth.

TREATMENT

This resolves itself into surgical and radium and X-ray therapy. Today our operability percentage is far greater than ten years ago. Inoperable cases are those with positive evidence of infiltration of the surrounding fat and muscle by either perforation of the wall or penetration through; also, the extensive involvement of the prostate and bladder base in the male. However, in the female, a fairly extensive involvement of the posterior wall of the vagina does not restrain us from operating. In the inoperable types one must search for relief of pain by making an artificial anus followed at times by the use of radium and X-ray. I regret that I cannot recommend either of these agents for cures, neither can I say they have held the growth in abeyance in any of the patients, barring one, a female, in whom I have had them used.

OPERATION

The operation of choice by me is the perineal. I find that none of my intelligent patients object to the perineal implanted anus as much as they do in suggesting the abdominal. I also find that the great proportion of patients with a perineal anus soon gain control by diet and timing their movements and are able to attend to their duties without soiling of the linen. One such patient, now in her seventeenth year following removal, has occupied the position of cloak model and saleswoman in a prominent department store since two months following the operation. She rarely soils herself—she is aware of an approaching movement. She has always thanked me for the perineal instead of the abdominal opening.

In forming an abdominal anus in the inoperable patients I am in the habit of making the opening in the sigmoid as low as possible, taking the chances of an intussusception, so that if we wish to use radium the growth may be reached readily from above as well as from below. Furthermore, the washing out of the lower loop is accomplished more readily.

There are instances when we feel that the lower portion of the sigmoid may be closed and dropped into the pelvis, leaving only the proximal end in the abdominal wall.

ANAESTHESIA

Spinal anaesthesia is my choice at the present time. I can get a quieter field below as there is not the tugging seen with general. The shock is exceptionally slight. The reaction is wonderful. The patient is able to take nourishment at his next meal hour and there is none of the after-vomiting pull on the perineum which we see with ether.

I do not attempt any of the many operative devices to act as sphincters, such as the Gersuny twist nor the splitting of the bundles of the *gluteus maximum* fibres but I rely on union to the surrounding tissues such as the *levator ani* and the ischio-rectal fats and fascia.

It does occur in occasional instances that the scar may contract so as to stenose. This may be easily overcome by doing a linear proctotomy or, preferably, if one observes contraction onset, the use of divulsing bougies is in order.

In the female the operation may be aided by splitting the posterior wall of the vagina or it may be necessary to involve the vagina if the growth encroaches upon it. The first operation in which I split the posterior wall was done in

1893, the woman living nine years with no rectal nor perineal metastases, but dying from a carcinoma of the uterine body and peritoneal metastases. About one year afterward, the late John B. Murphy of Chicago, published a paper on the vaginal approach to rectal carcinoma. This article was beautifully illustrated. The vagina is repaired after the removal of the rectum and the gut brought down and sutured to the then repaired perineum.

Outside of using the vagina in the female as a means of facilitating the removal, the steps are as follows:

The usual precautions as to bowel evacuations, blood chemistry, urine analysis, complete blood examinations and a preliminary low residue diet for a few days having been observed, the patient is placed in the lithotomy position and the field of operation and immediate surrounding tissues are painted with tincture of iodine. A small sponge soaked with iodine is introduced into the nondilated sphincter and rectum, care being taken against undue traumatization of the area to be removed.

The sphincter is then closed by grasping it in three towel clamps. These clamps will also be of inestimable value as a means of traction. The incision is then made through the skin and fascia, well outside the sphincter, exposing the ischiorectal fossa.

Traction is made through the agency of the towel clamps, bringing into view the levator ani and surrounding muscles. These are also cut through well outside the rectal boundary, care being taken above in the male to separate the prostate and deep urethra. Further traction is made, the fascia covering the rectum is incised, then by blunt and cutting dissection the rectum is free without difficulty, finger dissection is easily made in the sulcus of the coccyx and rectum, all restraining tissues are readily brought into touch or view and then can easily be cut between forceps, limiting the bleeding to a great extent.

Anteriorily the peritoneal pouch or *cul de sac* is readily demonstrated and may be opened if massive removal is called for. In the low situated growths I have not found it necessary to invade the peritoneal cavity. Nevertheless, it is an easy matter to remove the entire rectum and quite a few inches of the sigmoid after entering the cavity of the peritoneum.

Removal of the coccyx is unnecessary in the majority of these patients. Nevertheless, as its retention is not demanded, its excision will often facilitate the removal of the growth. When the growth is well out of the opening and an ample amount of normal gut is mobilized, clamps are placed distally and proximally to the point of excision. The gut is then cut between the clamps and, if possible, the wall of the gut is sutured to the skin margin, with drains placed properly. If unable to sew the bowel to the skin margin the forceps grasping the proximal gut are left on for forty-eight hours with drainage well placed, unless there follows a disagreeable abdominal distension. In such an event the clamp is removed within twenty-four to thirty-six hours.

In women the repair of the incised vagina is attended to before the final sutures between the gut and skin are applied. Should the clamps be left on, the vagina is then repaired with several added stitches in the perineum. Prolapse is a rare complication in this type of operation.

The age of these patients has included two under 35, the oldest has been over 71. So far the recurrences in these patients of mine have been in the margin of the anus, possibly implantation, but more likely the lymphatic involvement due to the fact that the lower set of lymphatics are subcutaneous and extend to the groin. Deep ischiorectal recurrences in two instances, one of each sex, were expected as the growths had perforated the walls of the rectum before operation. So far I have seen none with metastases in the abdomen, although all the cases have not been followed up. Vaginal involvement has occurred, evidently secondary to the primary invasion found at the time of operation.

All my patients have accommodated themselves very early to a gauze and cotton pad dressing.

SUMMARY

May I call attention to some of the essentials as to diagnosis and treatment:

1. In examining a patient place him or her in the lithotomy and not the Sims' position. By so doing the patient's anatomical relations are normal and a better compression of distance may be obtained by supra-pubic pressure, with the finger in the anus the perineum may be forced upwards. In this position the relationship of the pelvic organs is not displaced as in the Sims'.
2. Do not neglect the finger examination as the ordinary length finger will enable you to reach, with supra-pubic pressure, the recto-sigmoid growths.
3. Do not neglect examination by X-ray.
4. Do not neglect the proctoscope with the patient in the Sims', preferably the Trendelenburg position with the abdomen on the table or the lithotomy with the Trendelenburg position.
5. Do not overlook spasms of pain relieved by passing of gas or stool. This is a most important sign in conjunction with others.
6. Do not assign blood in the stools to hemorrhoids but be ever suspicious of a malignancy. This hemorrhoidal diagnosis has been the cause of many diagnostic errors and much chagrin to the hemorrhoidal diagnostician.
7. When in doubt always take a biopsy specimen. The picture by proctoscope and finger touch is positive in the majority of these growths although syphilis and tuberculosis are said to play a large part in rectal diseases. I have no record of a single case of either in the past ten years and but one case of tuberculosis of the sigmoid. There

is also the amoebic tumor. In the past year I have had two such cases, the result of the epidemic from and in the West.

8. Do not fail to search for caecal or colonic carcinoma in the presence of a marked anaemia. Too often these lesions are treated for a simple to pernicious anaemia over a long period before the diagnosis is made.

9. Lumbar, sacral and sciatic pains are frequent associates in lower colonic malignancy.

10. Do not put too much stress upon loss in weight as many sufferers from carcinoma of the colon do not lose weight until the disease is far advanced.

11. Ribbon stools are frequently seen in the normal colon and may be assigned to a spastic sphincter. When present in malignancy the growth is usually found in the anal zone.

12. Do not, in the presence of temperature and pain, reach out for some unusual disease but remember that a perforation with its associated symptoms and signs may be present and, too, temperature may be associated with a broken-down carcinoma.

13. Remember that diverticulitis may give all the symptoms and signs of a perforated carcinoma. However, in diverticulitis there is no marked anaemia, no loss in weight. The patient is usually well preserved, rotund and stocky, in apparent good health.

14. Do not rush to a conclusion without carefully reading the X-rays. I have seen the wife of a physician who had been operated upon for a gall-bladder disease because the spasm pain was not recognized and because the flat plate by X-ray showed a stone in the gall-bladder zone. Had the operator read the plates farther he should have readily seen a very great dilatation of the transverse colon and caecum with a definite splenic obstruction.

ABSTRACTS

MCGUIRE, D. PHILIP.

Carcinoma of the Colon. S. G. O., 59:762-765, November, 1934.

To avoid peritonitis, the greatest danger and most serious complication of surgical procedures for cancer of the rectum and colon, a preliminary cecostomy through a McBurney incision is advocated by McGuire, to be constructed two months before the actual resection. Low sigmoid and rectal cancers are then removed by an abdomino-perineal, one stage procedure, the peritoneal cavity being reintered after dissection has been completed first from above and then from below and the entire mobilized lower bowel, which has not been sectioned at any point, brought out of a left rectus incision to form a single "barrel" colostomy. The author suggests a novel aid in draining the cecostomy, viz: continuous suction.

Curtice Rosser, Dallas, Texas.

ROSSER, CURTICE.

Diothane in Surgery of the Anal Canal. S. G. O., 59:820-823, November, 1934.

A report is made of observations made on a total of two hundred cases of minor ano-rectal lesions operated upon under spinal anesthesia supplemented, in one-half the number, by local infiltration of "diothane," di-phenylurethane, to obtain prolongation of local insensibility.

The author is convinced of the relative absence of toxicity of the chemical under proper clinical safeguards, including preliminary barbaraturic medication and limitation of dose. The results in fissurectomy, ablation of thrombotic piles and other marginal conditions were quite satisfactory, anesthesia over a period of three days being common. Hemorrhoidectomy was not as satisfactory in the main as a field for this adjuvant anesthesia, although pain and necessity for catheterization were sharply lessened in most cases. Where distilled water was the carrier, instances of chemical abscess were encountered and delayed healing was possible. The use of isotonic solutions, with an optimum strength of one-half percent diothane, corrected this technical difficulty.

Author's abstract.

BEST, R. R.

Abdominal Incision in Lesions of the Rectum and Rectosigmoid as Related to Colostomy. S. G. and O., 59:194, August, 1934.

The writer prefers the left rectus incision, his own experience indicating that then hernia is not a sequella. Best also believes it preferable to re-enter the pelvis at a second stage through the original incision, rather than to make a new wound near by.

A very interesting suggestion is that clamps be applied at the time colostomy is performed and excess bowel removed with the cautery at this time rather than later; the clamp on the proximal vent is left in place several days.

Curtice Rosser (Dallas, Tex.).

HOLMAN, RUSSELL L., MAHONEY, EARLE B., AND WHIPPLE, GEORGE H.

Blood Plasma Protein Given by Vein Utilized in Body Metabolism. II. A Dynamic Equilibrium Between Plasma and Tissue Proteins. J. Exper. Med., 59:269-282, March, 1934.

An experimental study in dogs determining the effect of the intravenous injection of large amounts of blood plasma. Results indicate that even with high plasma protein concentrations, very little passes through the kidneys. If sugar is administered by mouth at the same time, nitrogen equilibrium is almost maintained, suggesting a give and take type of dynamic equilibrium between tissues and blood. Authors believe that in starvation tissue proteins of a different characteristic may be converted and utilized into blood plasma proteins.

Martin G. Vorhaus, New York, N. Y.

HOLMAN, RUSSELL L., MAHONEY, EARLE B., AND WHIPPLE, GEORGE H.

Blood Plasma Protein Regeneration Controlled by Diet. J. Exper. Med., 59:251-267, March, 1934.

A study of the effect on dogs of depletion of the plasma proteins by bleeding, after return of the washed red blood cells to the circulation. On a basal diet, the blood plasma proteins were kept constant by suitable exchanges close to the oedema level (3.5 per cent to 4.0 per cent). A reversal of the albumin globulin ratio takes place but the dog is kept in nitrogen balance, producing only about two grams plasma protein per kilo body weight per week. Prompt regeneration of plasma protein and the reversal to the normal ratio occurs with casein feeding, and even better with liver protein feeding.

Martin G. Vorhaus, New York, N. Y.

SECTION VIII—*Editorial*

The editorial contributions published in this Journal represent only the opinions of their writers. Such being the case, this Journal or the American Association is in no way responsible for editorial expressions.

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

THE "GRADUATE FORTNIGHT" ON DISEASES OF THE GASTRO-INTESTINAL TRACT RECENTLY CONDUCTED BY THE NEW YORK ACADEMY OF MEDICINE

MEDICAL organizations existing in our large cities might well give serious consideration to the annual "Post-Graduate Fortnights" which have become an outstanding feature at New York's Academy of Medicine — particularly if they wish to retain the interested (and dues-paying) allegiance of their members.

It is not necessary to emphasize that, in most of our major cities, the termination of the year's set schedule is accompanied by sighs of relief and feelings of gratitude by the Society's Officers. *Another* year has passed!

Another period of anxiety over what will or will not "draw" the "faithful few" but especially the discriminating, not easily *placeboed* many has been survived! *Another* Presiding Officer, *another* Secretary, *another* Program Committee now have the job and must face the demands of such members as still cerebrate in the modern *tempo* (the "past fifties" count for little: to them, almost anything which means a "meeting" at which they may talk "shop" suffices; they've held most of the "honorary" offices; frequently, age has relieved them of even dues-paying!)—how to arouse and keep the interest of the young "bunk" detectors, the up-and-coming-ers, the lads who expect new *pabulum*, thought-provoking theories or hypotheses, *real stuff:* that's the main concern!

It is no secret that for many years, despite all the pulmotoring of the paid (or voluntary) executives of so-called "organized medicine", the majority of our general or neighborhood medical meetings have meant "dates", not occasions for acquiring knowledge or receiving stimulation. Even "good fellowship" is lacking—as much now as before prohibition's repeal! If it be attempted, the suspicion arises that "politics" lies behind the effort. Programs exhibit deadening similarity year after year. Not infrequently they are arranged a year in advance, thus precluding discussions of immediate and pertinent problems. Speakers of local residence who may have real messages, all too often are not given "places" because of disharmony in institutional relationships or because "advertising" is frowned upon. "Guest speakers" widely recognized as "medical spell-binders" and crowd-drawers monopolize the programs, even though they have little to exhibit other than personality. The further the "guest" has to trek to speak his piece, it is assumed that the greater is his drawing power. If he be one who "made the boat" just before the gang-plank was pulled aboard and the fingers of a Hitler, Stalin or Mussolini clutched his collar, he "steals the show" even though, as he strides to the rostrum, baggy breeches flapping the tops of unshined boots, there sit before him local eminents, whom in his own country, he would address with crooked knee and dusty, black derby in hand!

"Duty", placement on "the honor roll", "nothing else to do", "curiosity", "politics", "to be seen", "not to be a slacker", occasionally a "desire to know what's going on," are reasons for attendance at meetings actually given on questioning.

"Subscription dinners"—particularly when the session is held at a well-thought-of club or a hotel famed for its *chef*—attract many and, if the bar be open, more. The meeting subsequent to the feast and the wassail is a minor attraction: a number never remains for it.

The situation is deplorable but it will not be improved by failure to acknowledge it. In the vast majority of our cities, and in extra-metropolitan areas, medical meetings are abhorred as thoroughly as are church or fraternal-society "fairs", "reading clubs", "welfare" or "uplift" gatherings, city, state or national political caucuses; only those who are pulling wires or are "in the game" for personal or institutional advancement or advantage are "keen".

Apparently, an individual or a group at New York diagnosed and appraised the true state of affairs some years since and having sized up the situation courageously set about to institute a form of treatment which held out hope for curing their own "sick" medical society. The remedy has proved to be as ingenious and satisfactory as was the initial diagnosis.

For seven years, under the really interested stimulus and the intelligent guidance of the capable official committees, annually, the New York Academy of Medicine has sponsored and carried through to successful fruition useful "Graduate Fortnights". These periods of concentrated effort in special fields of medical and surgical endeavor are a revelation to the physician accustomed to the cut-and-dried, humdrum, soporific medical meetings which have become "standard" in his community.

Perusal of the program of the recent "Fortnight" (October 22 to November 9), devoted to "Diseases of the Gastrointestinal Tract", demonstrates not alone the broad scope of the enterprise but a degree of intelligent planning, arrangement, co-operation and supervision which is a refreshing breeze into the dreary, ventilationless, smoke-befogged, carelessly formulated, time-wasting, commonly held medical gathering.

The Academy's fundamental idea of devoting a fortnight to presenting all phases of a special field of medical investigation, its laboratory aspects, diagnosis and treatment, is excellent. Last year it enabled the general practitioner, as well as the specialist in fields other than those of digestive diseases, in a brief period, to become acquainted with, and to estimate the worth of, present-day methods of research and clinical endeavor in digestive diseases. Further, the Academy, by being most catholic in spirit and broad-visioned, gives opportunity for any individual worker, who has worth-while material, to present it: all lines, so often drawn by personal prejudice, institutional jealousies, racial antipathies, real or fancied, schools of practice, are sundered.

As a result, one notes that some 180 individuals conducted hospital clinics, ward walks, laboratory demonstrations, exhibitions of new appliances and tests; more than 30 recognized authorities delivered formal evening addresses; there were 14 exhibits of rare or epoch-making books and incunabula, several unique displays of photographs and *curiosa* in gastro-intestinal art, 3 embryological and anatomical displays; 9 set-ups concerned with physiology and especially pathology; 7 exhibits dealing with the buccal cavity and the oesophagus; 14 devoted to the stomach and the duodenum; 2 demonstrating lesions of the small intestine (including complete exposition of Crohn and Ginzburg's syndrome, "Regional Ileitis"), 15 of the large intestine, 13 of the liver, bile passages and the pancreas, 15 of general gastro-intestinal tract anomalies, 6 concerned with tumors, 7 on amebiasis and allied conditions (including superb demonstrations by Mackie and Magath—Mayo Clinic—on amebiasis and by Felsen and Osofsky on Sonné dysentery), 5 dealing with the peritoneum, 4 on corrosive poisonings, traumatic lesions and foreign bodies, 3 on newer methods of laboratory diagnosis, 4 demonstrating newer technical procedures, 2 elaborating the significance of statistical data and 5 commercial assemblages of drugs useful in the treatment of alimentary tract ailments: a rather happy idea, since many physicians, although they are well acquainted with the applicability of advertised drugs, usually have very little personal familiarity with the appearance, physical properties, forms or of commercial presentation of such remedies.

Last year's "Post-Graduate Fortnight" while giving abundant opportunity for participation in its activities to physicians residing in New York's Metropolitan area, did not exclude speakers or scientific exhibitors from institutions in other cities. In the list of guests we find such authorities in their respective fields as Drs. Ivy (Chicago), Lewis, Lay Martin (Baltimore), Marriott (St. Louis), Magath, Mann, Bollman, Vinson (Mayo Clinic, Rochester, Minn.), Streeter (Carnegie Institute, Washington, D. C.), Babkin (McGill University, Montreal), Northrop, Kunitz, Herriott (Rockefeller Institute at Princeton), Cattell (Lahey Clinic, Boston), Casilli, Gerendasay (Elizabeth, N. J.), Pomeranz, Kraemer, Asher, Martland (Newark, N. J.).

Especially well chosen and arranged were the exhibitions of books and incunabula illustrating the progress of the knowledge of gastroenterology. Under the expert and discriminating knowledge of Drs. Archibald Malloch (Librarian of the New York Academy of Medicine) and Burrill B. Crohn, the Academy's Library was combed thoroughly for contributions in the general history of medicine which best illustrated the major advances of historical value in dietetics, anatomy, physiology, chemistry, special lesions, surgery and roentgenology of digestive diseases. In this country only a library so carefully assembled and so richly endowed as is that of New York's Academy could hope to display the important and unique works which were assembled. Doubtless, for the first time, many members of the New York profession became aware of the treasures which are in their midst. To the exhibition of books was added one of peculiar cultural interest, *viz.*, caricatures of gastrointestinal subjects in art—engravings and plates arranged by Dr. George L. Laporte.

It was most appropriate that, at a special session commemorating the 100th meeting of the New York Gastro-Enterological Association, Col. Fielding H. Garrison should deliver an address on "The History of Gastroenterology"—a Lecture with which the Journal expects to instruct and delight its readers in an early issue. Gertrude L. Annan exhibited certain Early Letters of William Beaumont Never Before Published. As equally appropriate from the historical aspect as was Dr. Garrison's address, was the choice of orator for the Wesley M. Carpenter Lecture, namely, Prof. A. C. Ivy, of Chicago, than whom no American investigator has contributed more fundamental studies concerned with Experimental Physiology. Safely, one may amplify this to "Experimental and *Clinical* Physiology". Prof. Ivy aptly spoke on "The Applied Physiology of the Gastro-intestinal Innervation"—a brilliant summary of present-day knowledge which appears in this issue.

It should be not necessary to add that this Seventh Annual "Post-Graduate Fortnight" of the New York Academy of Medicine was an outstanding success. Its clinical and scientific sessions were crowded with eager-to-learn practi-

tioners; its evening meetings brought capacity audiences; the special exhibits were busy gathering foci each day—places where, leisurely, men might study the new and the instructive groupings of the more or less well-known and where interchange of ideas and opinions meant far more than text-book reading or didactic teaching.

Modestly in his remarks the Academy's President, Dr. Bernard Sachs, voiced the fear that his Society might be accused of "advertising" by the holding of these Annual Post-Graduate Fortnights. Well, indeed, was he entitled, from the standpoint of the average general physician to add "but if this be *advertising*, make the most of it!"

The revivifying stimulus of this type of "advertising" would prove welcome and acceptable to dozens of medical groups scattered throughout the land. But, apart from New York, where does there exist the broad vision, the will to plan and work, the facilities for exhibition and instruction and, above all, the co-operative spirit which enterprises such as "Post-Graduate Fortnights" demand? Our profession is crying for this type of medical meeting but their yearnings fall on the deaf ears of so-called or self-nominated "leaders".

In view of the refusal of the New York Academy to permit a special section of "Gastro-enterology", it might be mentioned that the recent "Fortnight" concerned with Diseases of the Gastrointestinal Tract was by far the most successful yet held!

F. S.

EXPERIENCE WITH BLOOD TRANSFUSION WHICH ADDS PROOF TO THE VIEW THAT AFTER A MEAL THE BLOOD CONTAINS UNCHANGED PROTEIN

IN 1928, Brem, Zeiler, and Hammack (1) published a paper in which they pointed out that a patient with duodenal ulcer who, because of hemorrhage, had to have nine transfusions, discovered that he had uncomfortable febrile reactions only when the donor had recently eaten a hearty meal; when the blood was taken from a fasting donor, there was no reaction.

Recently, while chatting with Doctor Brem about this man and his experience, I found, as I suspected might be the case, that the patient is markedly allergic to food. He is so sensitive to beef that he cannot touch it. Shortly afterward, I saw an article by Price (2), who has made a careful study of these reactions following the transfusion of blood and who also has learned to avoid them by taking blood only when the donor is fasting. I find now that other physicians who have had a large experience with the transfusion of blood have learned to use donors who have not recently eaten.

What is needed now is to study the phenomenon more closely so as to see if the patients who react badly to transfusion from fed donors are ones who are highly sensitive to some foods. It would be interesting also to see if they react only when the donor eats foods to which they are sensitive.

Walter C. Alvarez, Rochester, Minnesota.

1. Use of Fasting Donors in Blood Transfusions. A preliminary report. Brem, W. V., Zeiler, A. H., and Hammack, R. W. Am. Jour. of Med. Sci., 175 (1) :96-103, 1928.
2. Diet of Donor as Possible Cause of Blood Transfusion Reactions. Rev. of Gastroenterology, 1 :192-201, 1934.

THE JOURNAL ENJOYS ITS FIRST BIRTHDAY

The present issue (February) completes volume one of the American Journal of Digestive Diseases and Nutrition. The response of the profession has exceeded all expectations and perhaps few special medical journals have got off to as good a start.

The editors are, of course, conscious of many shortcomings, but, with the excellent support enjoyed, these are being rapidly eliminated. Authors have been very generous. Readers have kept up a very helpful correspondence every month with the supervising editor. Circulation has expanded faster than we could have hoped for. Ethical advertisers believe in the Journal's value. Almost one-half of the internists in the United States and Canada and ninety-five per cent of the gastro-enterologists have subscribed, and good support has been gained from the busy general practitioners in every State in the Union.

Well-seasoned investigators, prominent clinicians, nationally known writers have flocked to the standard of the American Journal of Digestive Diseases and Nutrition. The editorial council have been much more than mere names, almost every member taking an active interest in the work. The American Gastro-enterological Association have not only honored us, but have been of inestimable help to us in our task of judging the temper of a wide reader audience. Above all, an ideal is being accomplished—medicine is being provided with a high-grade journal in an important field of study.

In the year ahead we plan to produce an even better journal. Provided our readers renew their subscriptions—a procedure which we heartily recommend—we feel that we can look forward to a long, and perhaps unlimited, future.

Beaumont S. Cornell, M. D.

SECTION IX—*Book Reviews*

(This section is open to contributions from any medical reader, whether a member of the Editorial Council or not.)

This Journal is not responsible for the opinions, decisions or grouping expressed by reviewers of books or pamphlets. For the guidance of readers, an attempt is made to indicate the relative worth of reviewed material by placing "stars"—★ in connection with the reviews. The greater the number of "stars," the more agreeably and importantly has the book or pamphlet impressed the reviewer.

★★★★ *Beitrag zur Kenntnis des Ileum Terminale Fixatum und Ileus Ilei Terminalis Fixati.* Peterson, Lennart; Helsingfors, 1934, Mercators Tryckeri Aktiebolag.

Here is a man who writes seven hundred pages on the fixation of the terminal ileum and the intestinal obstruction which sometimes results. He reports 120 cases of such obstruction which he found in the world's literature. It appears to be particularly frequent in Finland and is usually seen among men who do hard physical work. There is a bibliography covering sixty-three pages and abstracts of 217 case histories.

The author studied the cecal region in fifty persons coming to necropsy and reviewed observations made during 796 appendectomies. He agrees with other observers in stating that Jackson's membrane and Lane's kink are congenital in origin and to be found in 32 per cent of fetuses. No support was found for Lane's theory that the fixation of this region serves to suspend the cecum. The conclusion is that these membranes rarely produce symptoms and operations designed specifically to remove them should not be performed.

W. C. Alvarez, Rochester, Minnesota.

ABSTRACTS

RAVDIN, I. S.; RIEGEL, CECELIA; JOHNSTON, C. G., AND MORRISON, P. J.

Studies in Biliary Tract Disease. J. A. M. A., 103: 1504, November 17, 1934.

The excretory, secretory, and absorptive functions of the liver and the gall bladder and their associated ducts in health and in disease must of course be intimately correlated with the chemistry of the bile.

The bile has been studied in three groups of patients: (1) patients having chronic cholecystitis without stones, (2) patients having chronic cholecystitis with stones, and (3) patients having abnormal deposits in the gall bladder wall or lumen.

In the first group, the changes in the chemical composition of the bile is not very great although exceptions occur. In most of the specimens of the bile there was evidence of concentration of calcium or bile salt or both.

Of the patients in group two with stones, there are two types, those in whom the gall bladder was visualized after cholecystography, and in those in which the gall bladder did not become visualized. In the first of these groups, evidence of concentration of calcium and to a lesser degree of bile salts is present. In the second group, evidence of concentration of calcium and at times of bile salts were found but showed a great deviation from the normal. In the third group, the outstanding feature is the increase in the amount of calcium in the gall bladder. With the exception of those cases showing calcification of the gall bladder wall, the condition is associated with cystic duct obstruction.

There is no adequate explanation for the large amounts of calcium found in these gall bladders.

Studying human gall bladder bile found in operation and the chemistry of the stones found in the same gall bladder have shown little significant findings, because stones of different chemical composition are found bathed in bile of strikingly similar character, while stones of the same type are often found in bile whose composition is not similar.

In the acutely inflamed gall bladder with stones in which the cystic duct becomes obstructed, marked changes in the composition of the bile occurs. The greatest changes occur in the hydrops of the gall bladder in which the fluid removed has not the faintest visual resemblance to gall bladder bile.

In cholangeitis, the bile salt concentration of the liver bile decreases markedly. In common bile duct obstruction, either completely or partially, due to stone, tumor or cicatricial stenosis, the hepatic bile becomes altered in composition. The most profound changes occur when the obstruction is complete and the pressure in the bile ducts exceeds the hepatic secretory pressure.

The "white bile" found in many of these patients in which the parenchyma is no longer functioning normally results from the activity of the mucosal cells lining the ductal system.

Surgical drainage of the common duct is not often continued until the composition of the hepatic bile approaches anywhere the normal value. It is known that the loss of total bile for short periods rapidly may result in a profound salt disturbance of the body. The loss of bile salts is the important one, since they aid in the activation of various lipases and in emulsification and the transport of fat. Therefore, in cases where the hepatic bile is being drained, it is important to reintroduce a portion of this bile and this will greatly aid the patient's convalescence.

Francis D. Murphy, Milwaukee, Wisconsin.

SECTION X—*After "Hours"*

History of Gastro-Enterology

(With Special Reference to American Developments)*

By

COL. FIELDING H. GARRISON, M.D.

Librarian, Welch Medical Library

BALTIMORE, MARYLAND

FROM the time of Beaumont to the present, the physiology, pathology and surgery of the digestive tract have been not a little indebted to American enterprise and invention. In Germany, Kussmaul (1869), Leube, Ewald and Boas were the prime movers of recent developments. Boas was the first to specialize in gastro-intestinal disorders alone (1886), indeed started the first clinic and founded the first periodical (1896). The American Gastro-Enterological Association was founded in 1897, the German organization in 1914. Thus, a certain number of practitioners have been following gastro-enterology as a specialty for nearly half a century. Both Frerichs and Nothnagel stressed the backward condition of the subject in their time. Expansion was comparatively late, and mainly Germanic and American. This development had a long foreground and only the bare outlines of its history are known.

The interdictions put upon unsuitable, unclean or poisonous foods in the Mosaic code (Exodus, Leviticus) go back to the initial experiments of prehistoric man with regard to things edible or inedible. Everything was tried; much was learned from the avoidances of birds and animals; but troglodyte experience was often like that ridiculed in the English witticism about fox-hunting: "the unspeakable in pursuit of the uneatable." In some such way, dietetics became the basic element in ancient therapy. In the Hippocratic tract on Ancient Medicine (430-420 B. C.), human concern about diet is associated with the dim and dubious origins of rational medicine itself. To the primitive Greek (say of Hesiod's time), poisonous plants and animals were already matters of avoidance (taboo). Wheat, barley, fruit, wine and olive oil were the main vegetable staples. Meat was more extensively consumed in the Homeric period than later; fish little, if at all. From his own uncomfortable sensations, the Greek rustic learned, by long experience of trial and error, to prefer cooked food to raw; to restrict diet to an irreducible minimum during acute illness; to ease the sick stomach with slop diet; to defer eating until the subsidence of a fever; to strike a sensible balance between gluttony and abstinence. Farmers and day laborers, used to one, at most two meals a day, found themselves yawning, sleepy and stupefied after the novelty of a mid-day meal; with the common experience of flatulence, colic and diarrhoea, if a dinner followed the lunch. In the hands of peripatetic physicians, such rude initial data became the starting point of a rational semeiology and dietetic therapy, as expounded in the classic utterance of Celsus: "In this way, medicine arose from the experience of the recovery of some, the death of others, differentiating the harmful from the salutary things." The inference that rational medical practice originated in some such way has a high degree of probability; in other words, gastro-enterology is probably the oldest phase of internal medicine, dissociated, at the start, from supernatural (speculative) causes. That the primitive harvest hands made good experimental animals is reflected in the verse of Horace:

> "Edit cicutis allium nocentius,
> O dura messorum ilia." (Epode III, 3-4)

In early Greek pathology, the very efforts of the body to bring the humors from a raw, fermented status *(apepsia)* to normal *(pepsis)* were associated with the idea of cookery or coction, a view of digestive processes which survived until the 17th century. In the archaeological remains of ancient Egypt, concern about food is already that of a well-advanced civilization. We see the harvesting and marketing of fruit and grain; grape-arbors and fish-ponds; the kneading of dough; the brewing of beer; dining at table and the symbolic suckling of an infant at the udders of the cow Hathor. The Ebers Papyrus features intestinal parasites and the liver complaints common to all tropical and subtropical areas. In Assyro-Babylonian medicine, divination by in-

*Read at the one hundredth meeting of the New York Gastro-Enterological Association, Union Club, October 11, 1934, and reprinted through the courtesy of the New York Academy of Medicine.

Submitted December 2, 1934.

spection of the liver became an equivalent of prognosis. In the primer of Assyrian clinical medicine, which R. C. Thompson has pieced together from broken baked-clay tablets (1926),[1] there is already a respectable array of findings on diseases of the mouth alone. As assembled in the scholarly summary of Theodor Puschmann,[2] the practical knowledge of digestive disorders, scattered through the literary remains of Greek medicine, was not inconsiderable. True the clinical reasoning is clogged and obfuscated by the unbridled indulgence of the Greek physicians in speculating about the variable aspects of causation, by the general ignorance of human post-mortem appearances, by regrettable lack of the definite terminology necessary to classification, and by a pathetic groping toward clean-cut semeiology and therapy. Nevertheless, some of these clinical pictures of digestive disorders, embedded in the redundant expositions of Hippocrates, Celsus, Aretaeus, Galen and the Byzantine compilers, will be found to square with modern notions better than most.

The oesophagus, to begin with, while so denominated in Hippocrates, came to be envisaged as "the mouth of the stomach," the *cardia* of pre-Galenic writers. In Galen's time and thereafter, it was known as *stomachus*, both by the laity and the profession. By parity of reasoning, precordial distress *(morbus cardiacus)*, while allocated to the heart by Erasistratus, Asclepiades and Aretaeus *(syncope)*, was thought to be of gastric (eventually oesophageal) origin by Galen, Aetius and Alexander of Tralles. Caelius Aurelianus even differentiated a cardiac variety and a gastric variety, but the semeiology was necessarily obscure. Anorexia, excessive appetite *(bulimia)*, excessive thirst *(polydipsia)*, nausea and vomiting, sea-sickness and hiccough were all classified primarily as oesophageal disorders, yet recognized as symptomatic of gastritis and other digestive ailments. Diseases of the spleen and of the portal vein were long associated with the digestive system. Gastritis and hepatitis were recognized as such and handled at length, in separate chapters, by Aretaeus, Celsus and Alexander. Hepatitis might merge into jaundice, hepatic abscess or cirrhosis. The coeliac passion *(morbus coeliacus)* was a foul diarrhoea, associated with chill or atony of the stomach. Stools were sometimes examined in such conditions. The iliac passion *(ileus, volvulus, chordapsus)* was intestinal obstruction, often confused, for many centuries, with appendicitis. Diarrhoea, cholera, dysentery, ileus and painful stools *(tenesmus)* were allocated to the intestines. Colic was allocated to the colon. Intestinal ulcers were known. In the reading of Aretaeus, lientery (ridiculed in Molière) was a cachexia, usually associated with intestinal adhesions. Hippocrates and Aretaeus left masterly pictures of cholera, dysentery, jaundice and ileus. Alexander Trallianus notes three classes of intestinal parasites, viz., the thin, small worms causing anal pruritus *(Oxyuris vermicularis)*; the round worms in the upper bowel *(Ascaris lumbricoides)*; and the long flat worms, which often occupied the entire intestinal tract *(Taenia)*. thyme were employed as vermifuges. The test of expulsion was that of the young lady in Charles Reade's novel: "I see the vermifuge has acted." In the Alexandrian period, Erasistratus had already devised a rude calorimeter.

1. Thompson: Assyrian Medical Texts. London, 1926 (Englished in: *Proc. Roy. Soc. Med. (Sect. Hist. Med.), Lond.*, 1923-4, XVII, 1:1925-6, XIX, 29.
2. Th. Puschmann: *Alexander von Tralles*. Wien, 1878, I, 204-259.

For centuries, the theory and practice of digestion and its disorders was under the sway of the humoral pathology, in other words, virtually at a standstill. Beyond the dietetic precepts in the *Regimen* of the School of Salerno (1260), little was added to the practical knowledge accumulated by the Greek physicians. Associated with the four humors and the doctrine of planetary influences was the mediaeval theory of the constitution, centering in the four temperaments, viz., the sanguine (Jovial), choleric (Martial), phlegmatic (Mercurial) and melancholic (Saturnine). The bilious or cholaemic diathesis, attributing jaundice to yellow bile and a dour disposition to black bile, became basic in Arabic and tropical pathology, even down to the days of the peppery nabobs of the Anglo-Indian service. How little was added to the anatomy of the digestive tract before Leonardo and Vesalius is suggested by the terminology employed by Shakespeare and his fellow dramatists. In keeping with Greek and Roman usage, the stomach *(ventriculus)* was equated with the belly *(venter)*, as in the parable about the belly and the members in Coriolanus (I, 1) or the episodes of Falstaff and Justice Greedy (Massinger). Up to very recent days, the "fair, round belly with good capon lined" was regarded as a natural attribute of the elderly, who now obliterate the semblance of a swallowed watermelon by dint of golfing and banting. As depicted by Athenaeus, the Elizabethans and later writers, the capacity of the ancients, the English, the Germans and the Russians for food and drink seems beyond human credibility. Gluttony was early ridiculed in the bursting belly of Philoxenus (Athenaeus, viii, 341), which was plagiarized by La Fontaine *(Le Glouton)* and later by Pope:

> "The doctor call'd, declares all help too late:
> Mercy, cries Helluo, mercy on my soul!
> Is there no hope?—Alas!—then bring the jowl."

The drinking song in Gammer Gurton's Needle (1575) begins:

> "I cannot eat but little meat
> My stomach is not good,"

but a minute later, we have the reason, in the shape of a resounding chorus:

> "Back and side go bare, go bare,
> Both foot and hand go cold,
> But belly, God send thee good ale enough,
> Whether it be new or old."

There was manifest wisdom in the saw of the Persian poet Saadi that an empty belly connotes mental and spiritual activity or *vice versa*; whence the stomach, sometimes the whole gastrointestinal tract, were associated with animal pluck or courage ("guts"); fighting capacity with a full stomach ("Armies travel on their bellies") and the intestines, in particular, with compassion. Thus Wicliffe (1332) refers to the "bowels of Jhesu Christ", Sir Thomas Browne (1642) to "bowels of pity" *(Religio Medici)* and Jeremy Taylor to the "bowelless hangman" (1649). Even

in Bulwer's Eugene Aram (1832), we read: I am a man that can feel for his neighbors. I have bowels. I have bowels." The colon was sometimes equated with the stomach, e. g., "to feed colon" (Massinger, *Virgin Martyr*, III, 3) or Heywood's "What trick to satisfy colon?" The liver, for long regarded as the factory of the blood and one of the twin motors in the Galenic scheme of the circulation, was associated with courage, a touchy disposition and amorous propensities. Thus Hamlet (II, 2): "I am pigeon-livered and lack gall", or Chapman's "my venerean gentleman's hot liver" *(Widow's Tears*, 1612) or "I am all liver and turned lover", in an old play of 1606. The ancient fear attaching to a diseased liver in sacrifice and divination is reflected by Cassandra in *Troilus and Cressida* (V, 3):

> "Polluted offerings more abhorred
> Than spotted livers in the sacrifice."

Milton, Evelyn and Smollett describe a victim of congested liver as "liver-grown". Such expressions as "to stomach insults", "digest your angry choler" *(King Henry* VI, iv, 1), or to "digest the venom of your spleen" *(Julius Caesar*, IV, 3) are plainly survivals of an archaic physiology. In two places, Shakespeare maintains the old Galenic functional tripod of the heart, the liver and the brain *(Cymbeline*, V, 5; *Twelfth Night*, I, 1).

Up to the time of Beaumont, the physiology of gastric digestion was obfuscated by a series of dissolving views, summarized in William Hunter's epigram that the stomach was variously regarded as a mill, a fermenting wine-vat or a stew-pan.

To Galen, digestion was coction; in virtue of which, the stomach extracts what it needs from ingested food and passes on the rest to the intestines, the liver and other parts of the body *viâ* the blood channels. The mechanical view was advanced by Borelli and the Iatro-physicists, who limited gastric digestion to the grinding and crushing action of the musculature of the stomach. Baglivi even likened the teeth to scissors, the glands and viscera to sieves. The Iatrochemical theory of digestion as chemical fermentation was largely the work of Van Helmont, who maintained the old Galenic view that the products of digestion acquire natural spirits in the liver, which become vital spirits in the heart and animal spirits in the brain. Digestion is a continuous fermentative process in six stages. The acid, chyle-forming ferment in the stomach derives from the spleen. In the last stage, the tissues and organs absorbing the blood charged with vital spirits are envisaged as "kitchens." The stomach itself is the seat of the soul, since a knock-out blow at the solar plexus may destroy consciousness. The pancreatic duct was discovered by Wirsung (1642), the submaxillary duct by Wharton (1655), the parotid duct by Stensen (1661). Sylvius, therefore, stressed the rôle of the saliva, regarded both gastric and pancreatic juices as acid and may be credited with some vague notion of acidosis. De Graaf obtained saliva, bile and pancreatic juice from the dog by canalising the parotid, biliary and pancreatic ducts (1664). His work seems prophetic of Beaumont, as Brunner's experimental excision of the pancreas (1683) seems prophetic of Banting. Réaumur obtained gastric juice from the stomach of kites and demonstrated its solvent action upon foods outside the body (1752). Spallanzani confirmed those findings but denied that the solvent principle is an acid (1782). Young of Maryland proved what Van Helmont and Sylvius had surmised, that the gastric juice contains an acid, turning litmus paper red (1803). This acid Prout showed to be HCl (1824). Through an accidental window in the stomach, Beaumont, a year later, was able to view and describe the processes of gastric digestion and gastritis *in situ* (1825), noted the inhibition of digestion by emotion, constructed a dietetic table from the digestibility of different foods and thus created the true physiology of gastric digestion (1833). Gmelin and Tiedemann discovered tryptophan (1826), which Claude Bernard subsequently proved to be a by-product of pancreatic digestion. The Gmelin test for bile (1826) had been anticipated by Marabelli (1788). Purkinje and Pappenheim noted the proteolytic power of the pancreatic juice (1836) and Lucien Corvisart that this solvent action is independent of acidity or alkalinity (1857-63). Claude Bernard revived the experimental pancreatic fistula of De Graaf and demonstrated the rôle of the gastric juice in emulsifying fats, changing starches into sugar and dissolving the proteins passed on to the intestines from the stomach (1849-56). The conversion of proteins into peptones within the stomach was first described by Meissner (1859-62). Ptyalin was discovered and isolated by Mialhe (1845), trypsin by Willy Kühne (1876), biliverdin by Berzelius (1840); bilirubin by Heintz (1851); urobilin by Max Jaffé (1859).

Magendie first described the mechanisms of vomiting (1813) and deglutition (1817) but missed their reflex character, which was later elucidated by Kronecker and Meltzer (1880-83). Beaumont's observations on the movements of the stomach were confirmed in an excised preparation by Holfeister and Schütz (1886), but the real elucidation of this matter came from W. B. Cannon, who, at the instance of Bowditch, employed the X-rays (1896-1902). His findings are summarized in his book on The Mechanical Factors of Digestion (1911).

Cannon was the first to elucidate the mechanisms of gastro-intestinal digestion with X-rays and the bismuth (eventually barium) meal. He showed that the peristaltic wave travels continuously to the pylorus, with some slowing in the rate of conduction at the bridge, that the pylorus has an autonomy of its own in passing food on to the duodenum; that the pendulum movements of the small intestine (Ludwig, 1861) resolve themselves into rhythmic segmentations, to mix the content with the intestinal juices, culminating in a terminal peristaltic rush to the lower bowel; that the colon employs reverse peristalsis in the condensation of faeces and that the whole peristaltic process is affected by anaesthesia, surgical intervention, illness or other factors. Reverse peristalsis, contested by Mall, is a property of the entire gastro-intestinal tract. In 1912-13, Roger Glenard illustrated intestinal peristalsis, particularly during purgation, by the cinematograph. Alvarez, by means of moving pictures of the exposed digestive tube, has elucidated Cannon's findings in great detail, particularly *re* the doctrine of gradients (1914-18). Carlson has investigated in detail the hunger contractions of Morat (1882) and Boldyreff (1904-14), showing functional activity even in the fasting stomach, which becomes very painful in the cases of gastric ulcers. The net result of these findings is to the effect that the gastro-intestinal tract, like the heart, is an autonomic motor mechanism, which can function by the rhythmic, cell-to-cell transmission of impulse by the muscular tracts alone, even when excised from the body, and in which the nerve supply and intrinsic ganglia act as centralizers and co-ordinators in expediting conduction. Alvarez likens the co-ordinating nervous mechanism to a telegraphic or telephonic system attached to a railway or a factory, which can nevertheless run of themselves on occasion. The neurogenic theory of motor activity, which

Magnus set out to prove in the intestinal musculature, has been completely supplanted by the myogenic.

Pavlov did for the secretory activities of digestion what Cannon did for the motor mechanisms of the gastro-intestinal tract. His work covers the whole broad field of the effect of emotion upon digestion, merging logically into the doctrine of conditional reflexes and behaviorism.

Psychic secretion of gastric juice has been noticed in a gastrostomized dog by Bidder and Schmidt (1852) and in man by Richet (1878). But by combining the improved Heidenhain fistula with an oesophagotomy, Pavloff and his pupils were able to cover all aspects of sham meals and psychic secretions. Secretin, the intestinal hormone which activates pancreatic secretion, was postulated by Bayless and Starling (1902); enterokinase by Pavlov (1899). The bile-forming function of the liver was known to the ancients. In the Galenic view, the undigested material carried from the stomach and the intestines to the liver by the gross blood in the portal vein was converted into pure blood by the separation of yellow bile (carried to the gall bladder) and black bile passing to the spleen. The glycogenic function of the liver was discovered by Claude Bernard (1843-57). That the formation of bilirubin is associated with the disintegration of haematogen was known to Stadelmann (1890), Minkowski, Naunyn and others.

In 1913, Whipple demonstrated the possibility of extrahepatic formation of bile by excluding the liver *viâ* an Eck fistula. Mann proved this conclusively by excision of the liver (1924-5), showing that bile can be formed by histiocytes in the spleen, bone-marrow and connective tissue. This, one of the greatest discoveries in the history of physiology, is associated with the functions of the reticulo-endothelial system and the subsequent discovery of the treatment of pernicious anaemia by raw liver (1925-6). The metabolic relations of the liver and the other digestive organs is matter of vast extent.

Up to the 19th century, little of consequence was added to the knowledge of digestive disorders outlined by the Greek physicians. The most suggestive approach, the pediatric, was totally neglected, although the prevention of gastrointestinal disturbances in infancy, by breast-feeding, selection of proper wet-nurses and milk-tests, was well developed among the Greeks and the ancient Hindus.

The meconium was voided by placing a little honey upon the lips of the new-born (the sugar diarrhoea of Orgler). This practice continued up to the Middle Ages, when a bit of sugar or sugared baked-apple was substituted. In the 17th century, Walter Harris, a pupil of Sydenham, adumbrated the doctrine of acidosis in infancy, which he treated by chalk and pearl juleps. Apart from gout and dysentery, Sydenham himself has little to say of digestive disorders in the adult. Jan Heurne, memorable for his association with the beginnings of bedside teaching, left a posthumous pamphlet on diseases of the stomach (1610); Ferriol, a little book (1668). Martin Harmes wrote on diseases of the stomach and intestines (1684). A favorite theme of the 17th century physicions was the dyspepsia from gastric atony implicit in the title *"De imbecilitate ventriculi."* This usage continued into the 18th century, when it was sometimes equated with the "hectic stomach" (Arnold, 1743) and later with the *embarras gastrique* of the French clinicians. Swalbe (1664) published a lengthy satire on "the quarrels and opprobria of the stomach" *(prosopopoia)*. A more varied spirit of observation was manifested, here and there, by the 18th century physicians. In 1723, Boerhaave described a famous case of rupture of the oesophagus (autopsy on Baron Wassenaer). Pohl wrote on hardening of the stomach from abuse of alcohol (1771), Mertlick on intestinal sand (1786), Vanos (1704) and Lobé (1788) on diseases originating from gastric disorder. Congenital pyloric stenosis was described by Patrick Blair (1730), George Armstrong (1777) and, in America, by Hezekiah Beardsley (1788). Only two additional cases were recorded before 1888. Reil established the concept "polycholia" in 1782. Cowley had some notion of pancreatic diabetes in 1788. The literature on dyspepsia is large. The old doctrine of acidity *(De humore acido a cibo orto)* is reflected in Joseph Black's dissertation on CO_2 (1754). Friedrich Hoffmann published a long series of tracts an gastric haemorrhage (1679), saliva (1693-4) and its examination (1698), *Pumpernickel* (1695), apepsia (1696), diarrhoea in acute diseases (1700), gastritis (1706), diseases of the duodenum (1708) and the pancreas (1713), oatmeal cure (1714), iliac passion (1716), hepatitis (1721), diseases of the oesophagus (1722), cancer of the liver (1722), emesis (1725), pathology of liver diseases (1726), blood vomiting (1729), pharyngeal spasm (1733), and nausea (1733), which, if assembled, would make a very respectable manual of digestive disorders.

No such range of versatility in observation is apparent in any text-book between Hoffmann's period and that of Austin Flint (1868). The contents of early treatises on practice include no more than the diseases handled by the ancient writers, viz., dyspepsia, constipation, diarrhoea, colic, gastritis, enteritis, ileus, intestinal worms, jaundice, hepatitis and sometimes cancer of the stomach. A respectable fourth of Flint's Practice is taken up with digestive disorders and from this time on through the rest of the 19th century, there is farther expansion.

Among the earlier English books are those of Stone (1806), Marshall Hall (1820), Hare (1821) and Abercrombie (1828) on digestive disorders, Armstrong's pathological atlas of digestive diseases (1828), Rees on diseases of the stomach (1810), Howship on intestinal diseases (1820), Gibson (1801), William White (1808) and Faithorn (1814) on liver complaints. Later came George Budd's classics on diseases of the liver (1845) and stomach (1855), Brunton on diseases of the stomach (1859), which contains his account of plastic linitis, Frerichs (1858) and Murchison on liver diseases (1868). Contributions of enduring value were those of Laennec (1819), Hayem (1874) and Hanot (1876) on cirrhosis of the liver, Cruveilhier on the pathology of the peptic ulcer (1835), or Rokitansky's account of the pathology of acute yellow atrophy (1843) which Morgagni had described in 1762.

During 1867-9, Kussmaul began to employ the stomach tubes in the treatment of gastric dilatation and with this innovation, the modern development of gastro-enterology began. While stomach-pumps had been invented and employed by Alexander Monro (1767), John Hunter (1790) and Physick (1812) in the treatment of poisoning, this was a new departure. In 1871, Leube began to use the stomach-pump for diagnostic purposes, to experiment with test-meals and to envisage the concept "nervous indigestion", which was developed by Rejchmann (1883). Oser in-

troduced the flexible tube, which Ewald put into practice in 1875, combining aspiration of the gastric contents, with Boas' device of expression. Ewald and Boas then made test-meals viable. Ewald's Clinic of Digestive Disorders was published in 1879-88. Boas opened the first clinic (1886), began to lecture in the subject and published his text-book on diseases of the stomach in 1890-93. According to Bassler, he devised the resorcinol test, postulated the Boas-Oppler bacillus and the lactic acid and the high frequency of bleeding (95 per cent) in gastric cancer and used the test-supper to estimate gastric motility. Nothnagel's classic on diseases of the intestines and the peritoneum was published in 1896. From this time on, progress was rapid.

Mikulicz introduced gastroscopy and oesophagoscopy (1881). Glénard introduced diagnostic improvements (1885) and described the visceral ptoses (1887). Hirschsprung described megacolon (1887) first noted by William Leavitt (Chicago) in 1867. Bard and Pic described primitive cancer of the pancreas (1888) and Fitz haemorrhagic pancreatic necrosis (1889). Sahli is memorable for advances in diagnosis. Knowledge of jaundice and its modalities was forwarded by Weil (1888), Stadelmann (1891), Chauffard (1907), Widal (1907), McNee (1913-14), Inada and Ito (1916) and others; diseases of the pancreas and pancreatic diabetes by Mering and Minkowski (1889-93), Opie (1901-3); Ssoboleff (1902), Cammidge (1904); MacCallum (1909), Banting and Best (1924); biliary calculus by Naunyn (1892) and Aschoff (1909). The Plaut-Vincent angina (trench-mouth) was established in 1894-6.

Much light was shed by visceral surgery, which Naunyn described as an "autopsy *in vivo*".

Intestinal anastomosis, first attempted by the Salernitan surgeons, was brought to a high point of perfection by Abbe, Dean, Murphy, Halsted and Carrel. Billroth covered most of the alimentary tract through his resections of the oseophagus (1872), the pylorus (1881) and the intestines (1878-83). His pupil, Wölfler, introduced gastro-enterostomy (1881). In 1897, complete excisions of the stomach were done by Schlatter and by Baldy (United States). Lane's operation for intestinal stasis came in 1903. Marion Sims (1878) and Langenbuch (1882) excised the gall bladder. Maydl introduced colostomy (1888) and Kraske resection of the rectum (1892). Appendicitis, known to the mediaeval surgeons as *passio iliaca*, was early noted by Fernel, Heister and others; first operated for by Mestivier (1759); clearly localized by Fitz (1886) and standardized as to diagnosis and operative procedure by McBurney (1889). Subsequent operating on the gastro-intestinal tract by the Mayos, Weir, Deaver, Sands, Finney and other recent American surgeons has been brilliant. From the time of De Graaf, the physiology of digestion has been materially forwarded by surgical intervention on animals. Success in this field was naturally hampered by ignorance of the comparative anatomy and physiology of animals in the earlier centuries. Laterly, such procedures as Sander's device of exposing the intestines under salt solution for study of peristalsis (1871), the Eck fistula (1877), Pavlov's flap modification of the Heidenhain gastric fistula (1880) with intact nerve-supply (1900) or Mann's exclusion of the liver by excision (1921-5) have become essential and indispensable.

Röntgenography of the digestive tract owes much to the fluorescent screen and the Coolidge tube.

Holzknecht, Haudek and Groedel made the first worthwhile serial X-ray pictures of the stomach in man (1909-12). A. F. Hurst advanced the radiography of constipation and defaecation (1908). Graham and Cole made X-ray study of the gall bladder possible (1923-24). The sphincter of the common bile-duct (Oddi, 1877) was discovered by Simon P. Gage (1879). Non-surgical aspiration of the gall bladder, for diagnostic and therapeutic purposes, was introduced by Meltzer (1917) and Lyon (1919). Recent American work, at the Mayo Clinic and elsewhere, includes the investigations of Eggleston and Hatcher on the action of emetics and the mechanism of vomiting (1912-15), Case on intestinal stasis (1914-15), Alvarez on the mechanics of digestion and its clinical applications (1914-27), Ivy on gastric secretion (1920-25), Boyden, Mann and Higgins on the mechanism of evacuation of the gall bladder (1924-26). Einhorn introduced gastro-diaphany (1887), stomach and duodenal buckets (1890-1908) and duodenal intubation (1909). Fractional intubation of the stomach was introduced by Rehfuss (1914); functional pancreatic tests by Boas, Cammidge (1912), Einhorn, McClure and Bassler; hepatic tests by Ehrlich (1886-1900), Van den Bergh (1918) and others. Dietetic schemes for gastric ulcer were started by Leube (1897) and improved by Lenhartz (1904), Lambert (1908) and Sippy (1915). The bacteriology of the intestinal canal is associated with the names of Eberth, Escherich, Alexander Schmidt, Herter, Shiga, Flexner, Chalmers and Bassler.

The first independent periodical on digestive disorders was the *Archiv für Verdauungskrankheiten* (1895-6), founded and edited by Boas. Two years later, the American Gastro-Enterological Association was organized (1897), largely through the efforts of Aaron of Detroit. In 1914, Bassler founded the first American periodical, the *American Journal of Gastro-Enterology*. A section of Gastro-Enterology and Proctology was established in the American Medical Association in 1917. The New York Gastro-Enterological Association was organized on April 30, 1915, the National Society for the Advancement of Gastro-enterology in 1934. In connection with these developments, chairs were established in the principal medical schools of New York for Einhorn, Nesbitt, Kemp, Bassler, Kantor, Andresen, Chace and other leaders; of whom Aaron (Detroit), White (Boston), Simon (New Orleans), Alvarez (Mayo Clinic), Smithies, Carlson and Portis (Chicago), Rehfuss and Lyon (Philadelphia), Harris (Birmingham), Gerry Morgan and Verbrycke (Washington) and Soper (St. Louis) have been outstanding elsewhere (Bassler). Col. Seale Harris was in charge of the Division of Gastro-Enterology of the Surgeon General's Office during the World War. More recently, the Medical Department of the U. S. Army has organized sections of gastro-enterology in all general hospitals. The principal American text-books have been those of Einhorn (1896-1905), Hemmeter (1896-1901), Kemp (1910), Bassler (1910-30), Aaron (1911-15), Lockwood (1913), Niles (1914), Stockton (1914), Lyon (1923), Hurst (1924), Kantor (1924), Crohn (1927), Rehfuss (1927), Kellogg (1931), Alvarez (1931), Morgan (1931) and Buckstein (1932). As to disorders of infantile and adult metabolism, diseases of the blood and the nervous system, the dietetic treatment of all manner of clinical and surgical conditions, en-

docrinology and vitamin-therapy, the subject has immense ramifications, to which only passing reference can be made. In the light of these developments and of the work of Young, Beaumont, Fitz, Cannon, Mann, Whipple, Einhorn, Graham, Cole, Bassler, Alvarez and younger men, the record of American achievement in gastro-enterology seems far from contemptible.

During the long five-year famine, which followed the World War and the Russian Revolution, there was a gigantic turn-over of pathological conditions in Russia, which is of unique interest in connection with problems of food-economics, dietetics and gastro-enterology. Of old, the Russians were most liberal addicts of the pleasures of the table and, apart from communicable diseases, suffered mainly from disorders incident to repletion. There were dinners in pre-war Leningrad which were voted the best in Europe. At the International Medical Congress in Moscow (1897), few American physicians were equal to the banquet in wait for them, after negotiating the very lavish *Sakouska* of *hors d'œuvres*. During the famine period (1919-23), this dietetic set-up was literally upset. The disorders due to repletion were displaced and supplanted by disorders incident to depletion. Constipation, obesity, gout, diabetes, alcoholism, appendicitis, gastritis and liver complaints disappeared and gave place to anæmia, peptic ulcers, visceral ptoses, noma, pyorrhœa alveolaris, flatulence, meteorism, acute enteritis, gastric cancer, neuropsychoses and neurasthenia merging into sexual impotence, with an appalling mortality from diseases of the heart and circulation. In the darkest period, cannibalism was not infrequent, and there are rumors of another immense wave of starvation in the Ukraine latterly. At intervals, similar conditions have confronted the famine-stricken peoples of Ireland, China, India and Polynesia, of post-bellum Germany and Austria and those recently affected by the drought in our own Western areas. The famine medals of the Middle Ages are tokens of distinct heuristic value.

The immediate future of humanity will be largely bound up with economic problems, of which the relations of demand and supply in food-economics is one of the most outstanding. Facilities for transportation and administration, so essential to distribution of food-supplies of large cities and areas, have not been adequate to meet the problem of food-shortage. How intimately the medical profession is concerned with the economic problems of poverty, unemployment, food-shortage and starvation is suggested by the verse of Heine about the doctor whose sole prescription for an indigent patient was nourishing food and drink. From this point, our subject expands to the widest implications of the ancient saw, that man is and becomes what he eats *(Homo est quod est)*.

It is probably from this association with the good things of life that gastro-enterologists, like the pediatrists, are a very genial set of men.

PERIODICALS RELATING TO DIGESTIVE DISORDERS

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SECTION XII—"*The Clinic*"

High Rectal Pain Relieved by Elimination and Also by "Test-free" Diets*

By

DR. F. W. BRAMIGK, Ph.D., M.D.
DETROIT, MICHIGAN

RECENTLY, Bui and Brust, of the Mayo Clinic, reported an analysis of one hundred cases of high rectal pain.

In 71 out of their 100 cases, the cause of pain was not discovered. Self-observation in connection with research work about irregular forms of gout has taught me that one can control high rectal pains which have often awakened him at night by eliminating all food containing derivatives of wheat from his diet. This observation has been a peculiar, personal satisfaction.

Furthermore, patients coming in my office with like complaints of long standing were also almost immediately relieved when their diets were wheat-free.

Of two patients, one was relieved by Rowe's elimination diet and another who showed hypersensitiveness to some foodstuffs in Rowe's diet was relieved on a diet of the so-called "test" type.

In my own practice, I had previously observed in quite a number of duodenal ulcer patients, that so long as they were on milk and eggs only, or, finally, raw beef and milkrice, they were free of rectal pains, but the pain again appeared after giving them Holland rusk (wheat). Therefore, as a result of this observation, I have watched stomach patients for years for such hypersensitiveness.

Over one year since, after I had observed in myself a distinct hypersensitiveness for lentils (not until I had lentils in increasing quantities two and three times a day for three days, while on a purin-free diet over a period of more than four weeks), I submitted to food tests for hypersensitiveness at the hands of an allergy specialist. No positive response was noted. Last summer when by observation, my wheat hypersensitiveness was well proved, I did not react on intradermal test until I had eaten wheat repeatedly. Eight days later, the point of injection at my previous allergic test study reacted by itching after drinking a certain beer; probably this beverage contained wheat in some form.

The rectal pain was frequently described by patients just as personally I had experienced it. First, a degree of pressure inside of the rectum which, as it were, "gave the signal"; shortly afterward, this distress slowly increased until suddenly it became an actual pain: as though a sharp-pointed instrument had been pushed into the rectum, quite high up. When first I experienced this pain, it felt as though some sharp-edged object had been swallowed (a fish bone, a fruit seed, etc.), which moved through the intestinal tract and finally had become held at the recto-sigmoid valve.

Patients repeatedly say that there is "a feeling of a sharp stone up there". They attempt to dislodge "the object" by moving the bowel, but all to no purpose. Soothing or anti-spasmodic suppositories usually give relief.

CASE REPORTS

Case 1—Male 41 years, complained of constipation, "always a nervous stomach", used to have hunger pains, but is relieved after eating and by diet; still some sour stomach and bloating; sharp burning pain and sensation of fullness in the rectum commonly at night; "at the same time the nose blocks up"; the tongue is heavily coated; at times has aching in knees and ankles and has sacro-iliac pain. The patient consulted different specialists for rectal examination; his findings were negative. He received prostatic massage for a long time; a year ago when on a buttermilk diet the condition became worse.

Rowe's "elimination diet" relieved him immediately, and only once, when going off the diet by eating ice cream, did he experience a set-back.

Case 2—Male 51 years, complained of severe headache and "stomach trouble"; two to three times a year has had severe vomiting spells for the past thirty years. For ten years has had pain in rectum; rheumatic pains in legs, and for one year blurred vision; felt unsafe at work lately. He stated, "When I sit at the table I feel like eating a large quantity but while still eating, I get a pain in the rectum and have to run to the toilet. The bowel movements are, at times, like small bullets; at others flat, but when I feel entirely well the movements are of normal size and shape". He has five to six small movements daily, mostly watery. The patient has had X-ray, proctoscopic and sigmoidoscopic as well as cystoscopic examinations and all have been negative. He showed skin hypersensitivness for many foodstuffs and especially to wheat, rye, barley, corn, olive oil, beef, eggs, string beans, spinach, asparagus, carrots, potatoes, tomatoes, lettuce. He

*From the Department of Internal Medicine, Central Medical and Dental Group.
Submitted November 11, 1934.

was placed on a diet consisting only of rice, tapioca, milk, lamb, sugar. Four days later: normal bowel movement, no pains in rectum, "sick feeling" has gone, blurring of vision has improved; slept better. Stated that he felt safe at work. The diet was increased by addition of pumpkin, squash, apples, pears, buckwheat, cherries, apricots, almond, cocoa, trout, bass, halibut, raw smoked ham, all for which he exhibited negative skin tests. I saw him again 8 days later, he was feeling well and not so nervous. Duck and lamb were added, and after another week, potatoes, tomatoes, lemon, orange, veal and oysters. I saw him twice more, the last time recently. Forty-two days after the first visit he had a normal bowel movement, no more headache, sleeps well, stomach digestion apparently normal; occasionally has slight dizziness. Urobilinogen which was first 4 + now is normal. Apart from the diet, the patient was given belladonna and a saline cathartic.

In our experience, Rowe's "elimination diets" and his medication have proved very helpful especially where time or financial circumstances did not permit extensive skin testing.

It is not our practice to depend on the result of the skin tests alone; not infrequently such tests give false negatives. Apart from the dietetic relief of certain types of obscure high rectal pain, our observations indicate that elimination diets or what one may style "test-free" diets, may prove of clinical value in the management of "irregular" forms of gout, particularly that group where abdominal pain is an associated symptom.

Dystrophia Adiposogenitalis and Its Related Disturbances*

By

C. VICTOR RICHARDS, A.B., M.D.
BALTIMORE, MARYLAND

THIS syndrome introduced by Froelich is but one type of obesity having its roots deeply imbedded in the endocrine glandular system and the autonomic nervous system, the manifestations of which incriminate more than one of the endocrine glands. Thus, it is seen, that an imbalance of the endocrine system is capable of various clinical pictures of fat metabolism and though we present to you ultimately a fairly typical case of this Froelich type, the chief endeavor will be to draw attention to the significance of general considerations underlying not only this type but various other disturbances in which fat metabolism is concerned.

One needs but call attention to the recent advances[1] in the discovery of the more important secretions or "autocoids". It is apparent that these secretions are balanced in their function.[2] Furthermone, it would appear from a perusal of the literature since Falta's exquisite treatise on the subject that the autonomic nervous system functions, balanced on the one hand by the cranio-sacral autonomic, and on the other hand by the sympathetic nervous system.[3]

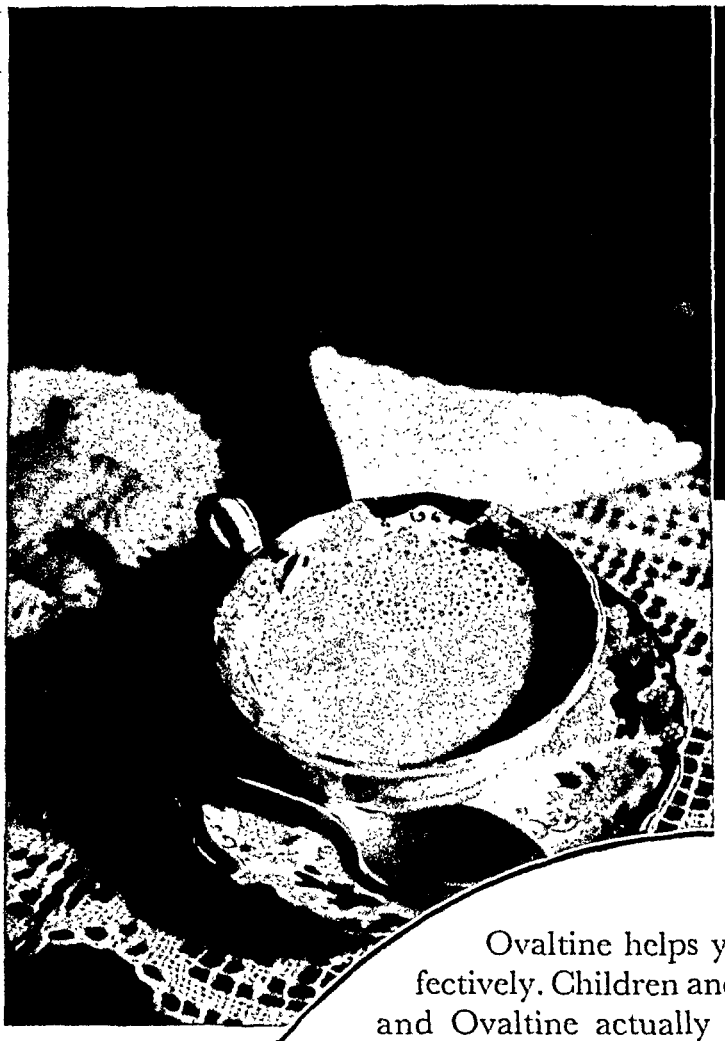
For this nervous system to function without consideration of the glandular system would be a paradox. The one seems to be a projection field of the other.[6]

Our daily use of vagimimetic and sympathomimetic drugs is but a clinical acceptance of this significance while in the actual glands themselves we find even more powerful hormones and *chalones*.[4] From out of the close hook-up of these two basically important tissues we have secured the following useful agents: "Antuitrin" from the anterior part of the hypophysis is credited with the control[7] of growth and sex function while "pitocin" and "pitressin" from the posterior part are stimulants of smooth muscles, the former without the pressor activity and the latter with it. "Thyroxin" is now a well-known therapeutic agent in hypothyroid conditions. Adrenalin and cortin[5] from the medulla and the cortex, respectively, have proved to be quite as great discoveries as was insulin. This latter substance in the control of diabetes has opened up avenues of research which point to the importance of the mechanism existing between the autonomic nervous system and the endocrine glandular system. For example, adrenalin facilitates the mobilization of liver glycogen while insulin regulates the consumption of sugar by the tissues. The female sex hormone[7] which experimentally controls the *estrus* cycle bids fair to become a very powerful agent in gynecological practice. Not one of these potent extracts can be administered without immediate or remote physiological effect upon the autonomic nervous system.

GENERAL CONSIDERATIONS

If, therefore, we digress from the particular kind of fat dystrophy indicated in the title to a consideration of a background[4] which *envelops* this not uncommon malady; that digression, we trust, will be tolerated in order that we might the more readily reach out and draw in the loose threads of some very common medical and surgical entities, such as the abdominal triad.[8] This picture of *adiposogenitalis* when scrutinized for details is a very unsymmetrical fat female under forty, humorous in youth, pathetic in adult life. But, when studied in its more abstract environment, the picture gradually becomes a focal point in the background and finally one sees it encircled with a halo of recent discoveries. One might brand it a mere coincidence that the anomaly has associated with its fat disturbance two elements of the abdominal triad whose component parts[9] are appendicitis,

*Read before the Baltimore Medical Society. Submitted November 13, 1934.



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ulcer, and chronic cholecystitis.

We think that the literature will bear out the statement that this patient is fat, asymmetrically proportioned, possessing infantile sex organs, suffered appendectomy and cholecystectomy for much the same reason that she ran the gauntlet of acute infections; namely, an unbalanced endocrine and autonomic nervous system.[10] Therefore, for us to tinge cold abstractions with the warm hues of imagination is at least tempting. Before the naked reality of cortin, adrenalin and insulin was seized upon, the gorgeous display of mystic fancy clothed it. And thus throughout medicine we see the guesses of mysticism being clothed in later years by the realities of science.

Recent literature discloses a few pertinent considerations: the age incidence[9] of appendicitis, ulcer and gall-bladder infection in this order is significant, so also is the fact that analogous proliferative and reparative changes in the tip of the appendix and the neck of the gall bladder accompany subacute and so-called chronic appendicitis. That infected "B" and "C" bile not infrequently are accompanied by a chronic appendix or evidence of its removal because of previous attacks, is an accepted fact. *Ulcer* has been both caused and retarded by interference with the endocrine and sympathetic balance;[4] furthermore, the appendix is considered in over 80 per cent of ulcers to have been the culprit.

Dr. Deaver's alliteration of "fair, fat and forty" has become synonymous with gall-bladder disease and this is of *glandular* concept. Dr. Draper's[11] "ulcer facies" is basically a neuropathic concept. The mixed notions[12] about the etiology of appendicitis are due to the lack of developed visible characteristics in the young which has not been made manifest by the nerve and glandular imbalance.

We venture the assertion that if "B" and "C" bile were cytologically and chemically studied in all cases of acute appendicitis, that instead of merely *feeling* and *looking* for *macroscopic* evidences of disease one would find considerable evidence pointing to the early involvement of the gall bladder and the hepatic radicles.

It is decidedly wrong for the surgeon to proclaim a gall bladder normal simply by inspecting it. Its transport mechanism might be normal and its appearance also, but before this all comprehensive word is used, a study of the bile fractions, particularly "B" and "C", should be made.[13]

It is equally fallacious also for one to presume that because a gall bladder's transport mechanism is normal by the Graham-Cole visualization procedure that its contents are normal. The writer[13] frequently finds evidences of first or second degree gall-bladder lesion by the non-surgical drainage method when, roentgenologically, the visualization of this reservoir discloses a normal transport mechanism. The only accurate estimate of the gall-bladder pathology without excision is by repeated non-surgical drainages.

The initial steps of this organ's involvement are seldom encountered by the surgeon and will continue to be ignored by the patient since the symptoms are not sufficiently portentious; an occasional right upper quadrant discomfort with a suspicious attack of appendicitis usually is deferred until the appendicitis calls for surgical interference. At this period of the disturbance one may expect to find intubation evidences of intra-hepatic and gall-bladder disease.

Dr. Deaver[20] has recently called attention to the changes taking place in liver and lymph channels, *apropos* of gall-bladder disease, and the necessity of early interference to forestall permanent hepatic damage. It is in this stage that assured emptying of the gall bladder by repeated drainage proves therapeutically advantageous.

Apropos of the endocrine significance, we will relate to you some outstanding figures which Lawrence and Rowe[14] published in "Endocrinology". They found in the examination of 4,000 cases (particularly on the outlook for endocrinopathic disturbances) that, in the *thyroid failure* group the gastro-intestinal positive findings and liver dysfunction positive findings, were 40 per cent. These findings were based on gastro-intestinal X-ray series, duodenal analysis, functional liver tests, Van den Berg reaction, and glucose tolerance test. A similar percentage was found in the pituitary group. In 1,000 females in the primary endocrine cases there was a 4.6 per cent rate of gastro-intestinal complication and a 16.4 per cent for liver and gall-bladder disease. Contrast these figures with those found in non-endocrine group: 3 per cent for gastro-intestinal complications and 2.6 for gall bladder and liver. We find the thyroid and the pancreas (also the adrenals alone) contributing twice the amount of pituitary and gonad cases. Marinus and Kimball[15] found 18.6 per cent of 3,500 school children were victims of endocrine deficiency, thyroid and pituitary predominating.

Sheppard Schapiro[16] reports a frequency of incidence of *adiposo-genitalis* in which he found 45 out of 1,800 pupils of the Froelich type; while 2.5 per cent of these 1,800 pupils had definite endocrine disturbances. If we remember that "the first subnormal state which evolves, is a retarded mentality; and as puberty develops, hypogenitalism becomes more prominent, and the fat dystrophy usually continues into adult life", obviously then the time to observe the beginning of these syndromes is in early life. It appears to us, therefore, that this "abdominal triad" also has its beginning in youth around the adolescent period according to the age incidence figures.

The question arises: will we find on closer scrutiny that the first attacks of appendicitis really are occurring in constitu-

tions which also show some endocrine imbalance? If so, this throws considerable light upon the deductive findings of Deaver with respect to the gall bladder and Draper respecting ulcer.

Disturbances in basal metabolic rate do disturb the defensive mechanism. Perhaps this is the reason for the myriad infections such individuals experience.

To prophesy would be unscientific; but as one mulls over the literature and endeavors to organize figures and theories, one can scarcely miss seeing the red thread of ripened disease as it spots the background of the black and white threads of mysticism and science, which are being woven into the fabric before us.

To administer simply atropine, adrenalin, and other vagimimetic and sympathomimetic drugs, as the case might demand, has proven useful. How much more useful then are these pure hormones in the hands of the experienced physician?

A year or so ago we were confronted with the following history and physical findings:

CASE HISTORY

Complaint—Obesity, muscular fatigue, repeated infections, left hypogastric pain with bloody stools, constipation, alternating with frequent attacks of diarrhoea, bloating and distension after meals; occasional oedema of the ankles.

Family history—Mother's sister weighed 300 pounds; brother, 250 pounds with diabetes and chronic gall bladder, and chronic appendix diseases.

Personal history—Tonsillitis, abcessed teeth, otitis media, mastoiditis, influenza, diphtheria, pneumonia, appendectomy and tonsillectomy in a female patient twenty-five years old!

Physical examination—C. V. R. system: essentially negative.

G. I. system: chronic cholecystitis, diagnosed both by the non-surgical drainage method (which showed pathognomonic signs of infected "B" and "C" bile with a constant hyperacidity on fasting analysis; with a normal transport mechanism of the g. b. after cholecystography), and by the g. i. series which showed a colitis with spastic sphincters. *Proctoscopic examination* confirmed the colitis. *G. U. system:* infantile uterus, delayed and irregular menses; no urinary disturbances. Glucose tolerance test not made.

In general the patient is a thickset Jewess, weighing 273 pounds, 5 ft. 6 inches high, who two years ago showed −18 BMR. *Trophic disturbances:* hair, nails and their crescents and the skin showed moderate suggestive evidence of hypothyroidism. Fat distribution: scapular, trochanteric, gluteal and thigh regions, with a very prominent "penniculous adiposus" over the abdomen, all of which were out of proportion to the neck, forearms, and lower legs, which did not share in this obesity. *Skeletal system:* there was a moderate maxillary prognathism, marked genu-valgum with tapering fingers and a general asymmetry. Homologous sites of body areas differing by several centimeters.

COMMENT

The anterior pituitary element experimentally appears to produce two hormones, namely, the growth hormone which decreases the metabolic rate and increases the specific dynamic

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action of food, that is, influences metabolism while the sex hormone ripens the follicle and enhances leuteinization. Happily there is then some scientific justification for the use of antuitrin and thyroid in this particular case. The thyroid as is known causes rapid mobilization of liver glycogen by the liver cell and facilitates combustion in the tissues.

Therapy:[17] Hormones of the anterior pituitary body were given *t. i. d.*, and every other day one ampule of the extract called autuitrin. Thyroid extract was given to tolerance *t. i. d.*; nonsurgical drainage of the g. b. weekly and an autogenous vaccine of the non-hemolytic streptococcus. The diet was predominantly base forming.[18]

Results: At the end of seven months this patient lost 70 pounds, but had a gall bladder attack, which organ was immediately removed. She constantly improved subjectively and objectively. One year after treatment she was remeasured, and she showed approximately normal proportions with bilateral symmetry. Furthermore, she has been more resistant to infections, has lost entirely the abdominal apron, and is free from colitis and continues to menstruate regularly.

Discussion Notes by Dr. T. B. Futcher: There has been a general impression that the syndrome known as "dystrophia adiposogenitalis" is associated with hypofunction of the anterior lobe of the hypophysis. It is interesting to note that Camus and Roussy, and Bailey and Bremer of Harvey Cushing's clinic, in their experimental studies on animals in connection with the cause of diabetes insipidus, found that the latter disease could be produced by punctures of the hypothalamic region in the vicinity of the tuber cinereum, and that some of these animals (dogs) developed signs of dystrophia adiposogenitalis.

It is well to remember that the anterior lobe of the pituitary gland yields growth and sex hormones. This lobe contains three types of cells, chromophile (eosinophilis), chromophobe and basophilic. Many are of the opinion that hyperpituitarism (gigantism and acromegaly) are due to adenomata involving the acidophilic cells, and hypopituitarism *(dystrophia adiposogenitalis)* to adenomata in which the chromophobe cells predominate. The sex hormone is believed to be produced by the basophilic cells.

Discussion by Dr. Emil Novak: Dr. Richards' interesting paper brings before us a subject which makes points of contact with all branches of practice. Adiposogenital dystrophy is certainly one of the most common conditions encountered by the gynecologist, chiefly because of the characteristic menstrual disorders associated with it. The obesity, as is well known, is of rather characteristic type, with heavy deposits about the shoulders, busts, adbomen, hips and buttocks. There has been much discussion as to whether the adiposity, like the menstrual anomaly, is due to a hypofunction of the pituitary, or whether it is produced by some other factor. The recent work of Philip Smith has apparently settled this question, this investigator having shown that the metabolic disturbance responsible for the adiposity is due, not to any pituitary disturbance, but to a disorder in the adjoining hypothalamic area of the brain. In spite of this fact, the menstrual disorder and the obesity are so characteristically associated that the syndrome, in spite of Smith's work, will probably continue to be spoken of as adiposogenital dystrophy.

The treatment is, of course, still unsatisfactory. Thyroid extract is still the sheet anchor, with efforts at ovarian therapy along still rather unsatisfactory lines. Some excellent clinicians employ anterior pituitary substances, often orally, but I do not believe these accomplish results without the thyroid. Perhaps the newer physiology of the anterior hypophysis may before long indicate a more direct and more satisfactory line of treatment.

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S. W. CLAUSEN.

Physiological Reviews. The Influence of Nutrition Upon Resistance to Infection. 14:309-350, July, 1934.

Clausen points out that the possibility that diet may have some influence upon the incidence, course and final outcome of infection is a comparatively recent idea. The absence of pure preparations of vitamins for experimental purposes has hindered progress in this field which appears still to be in its infancy.

The conclusions reached are that *susceptibility* to infection is not as a rule affected by diet while *resistance* to infection, on the other hand, greatly may be reduced by deficient diet. A deficiency in the diet of vitamins A and C appears quite definitely to lower resistance to infection. In certain cases, lack of the vitamin B complex also may do the same thing. A lack of vitamin D cannot be said to have a proven effect in lowering resistance. It seems probable that the existence of a partial deficiency of vitamins may result in loss of resistance to infections, though this cannot be said to have been clearly established from evidence yet available.

Dwight L. Wilbur, Rochester, Minnesota.

NECHELES, H., AND SCHEMAN, L.

Detection of Free Acid in Patients with Suspected Anacidity. J. A. M. A., 103:107 (July 14), 1934.

The authors describe a method of testing the acidity of the stomach contents while it is passing from the stomach tube to the container before filtration. They have developed this method because they have been impressed by a number of cases which showed a positive Töpfers reaction for free acid before filtration while the same sample after filtration showed no free acid. Their explanation is that the slight amount of free acid present combines quickly with the mucus present or is neutralized by duodenal regurgitation. They illustrate and describe in detail the method which they have utilized for the detection of free acid in such cases.

Francis D. Murphy, Milwaukee, Wisconsin.

THORSON, J. A.

Nutritional Xerophthalmia. J. A. M. A., Vol. 103, No. 19, Page 1438; November 10, 1934.

Thorson reviews some of the literature on nutritional xerophthalmia and he records another interesting case of this condition in which the disease ran a protracted course for six years with seasonal variations in severity. During the fall and winter months when the patient consumed no Vitamin A the disease was worse, while in the spring when a few green vegetables and eggs were eaten, sight was better.

The author remarks that the effect of abundant sunlight, as already pointed out by others, must also have been an important seasonal therapeutic factor.

Samuel Morrison, Baltimore, Maryland.

TUCKER, GABRIEL.

A Method of Roentgen Localization of Foreign Bodies in the Stomach Prior to Gastro-scopic Removal. J. A. M. A., Vol. 103, No. 19, Page 1440; November 10, 1934.

Tucker outlines a new method of localization of foreign bodies in the stomach. He passes a rubber tube and allows it to remain in position during the making of films, the patient being placed in the position required for gastroscopy.

Tucker summarizes the advantages of this method as follows:

1. It shows the location of the foreign body with reference to the tube that is passed into the stomach.
2. The tube stays in the lower part of the esophagus and cardiac end of the stomach and gives a definite localization of the foreign body to the cardiac end of the stomach, where the gastroscope is to be introduced.
3. The rubber tube is withdrawn and gastroscopic removal can be proceeded with immediately.
4. The stomach contents can be aspirated and air introduced if desired before the tube is withdrawn.

Samuel Morrison, Baltimore, Maryland.

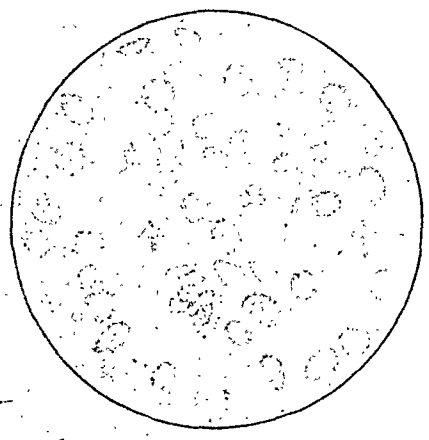
SNELE, ALBERT M., AND CAMP, JOHN D.

Chronic Idiopathic Steaorrhea. Roentgenological Observations. Vol. 53, No. 4, April, 1934, p. 615.

A further report bringing the total to seven cases, is made by the authors on this interesting and infrequent association of fatty diarrhoea with changes in the metabolism of calcium and phosphorus. This condition resembles tropical sprue and has also been referred to as "adult celiac disease". The duration of the reported cases varies from six months to a life-long period. The periods of diarrhoea are accompanied by loss of appetite, flatulent indigestion, loss of weight and active tetany, the latter occurring over a period of very many years. The patients are usually markedly emaciated, pale, present in some cases a glossitis, atrophy of the tongue, abdominal distention and bony changes as kyphosis, bony contractures and other signs of osteomalacia. The calcium and phosphorus in the blood are generally reduced, the urinary excretion of calcium low but the fecal high.

The roentgenological studies in three out of seven cases revealed delayed motility and mucosal alterations in the small intestine, especially the jejunum, as smoothening of the contours of the lumen, obliteration of the usual markings of the *valvulae conniventes* and clumping of the barium in elongated masses, suggesting an inflammatory condition.

The cause of the symptoms has been ascribed to disturbances in the absorption of fat in the intestine which in turn prevents proper assimilation of calcium and phosphorus from the ingested food. The authors quote Bauer, who believes that among other possibilities, the question of



ANEMIA caused by bleeding gastro-duodenal ulcers requires caution in the selection of the iron treatment, which must be non-irritating.

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deficient external pancreatic secretion must be considered.

Several suggestions as to treatment are offered. Rest of the alimentary tract is important and is obtained by dietary regulations and a high protein intake. Many of these patients cannot tolerate a high fat intake. Vitamin D, parathyroid extract (Collip), as a symptomatic remedy, calcium medication, and an antianemic regime are recommended. The authors advise an evaluation of the most important etiologic factors and direction of the treatment accordingly.

Leon Bloch.

ROSS, LLOYD I.

Carcinoma of the Rectum in Youth. Report of three cases. Am. Jour. Cancer, June, 1934.

In the June issue of the American Journal of Cancer, Lloyd I. Ross presents a very interesting article on a timely subject entitled "Carcinoma of the Rectum in Youth." He reports three instructive cases, seeking to prove that carcinoma of the rectum is not a disease limited to the declining decades of life.

The first case relates to a 21-year-old white female whose chief complaint was massive hemorrhage from the rectum; one and one-half years prior to entry, the patient had been to the City Sanitarium because of pulmonary tuberculosis, and a later examination showed a large, irregular growth involving the anterior rectal wall, and apparently encircling the rectum about six cm. above the anal orifice. Post-mortem examination revealed an ulcerative stenosing adenocarcinoma of the rectum, and a recent diffuse seropurulent peritonitis, but no gross perforation of the intestine was found. In addition, there was an encapsulated caseous tuberculosis involving the right middle and lower lobes, and a tuberculous bronchopneumonia on the left side. This case is of particular interest because of the coincidence of a malignant tumor and pulmonary tuberculosis. The author seeks to counteract the idea in the lay mind at least, that persons with tuberculosis are protected from the ravages of cancer; he quotes Wilson and Mayer to prove that slight positive association exists between the two diseases.

Case two is that of a 21-year-old white male, the chief complaints being fullness in the abdomen, diarrhoea, and loss of weight. It was thought that the symptoms were due to a small umbilical hernia, which was repaired. A month later, exploratory operation revealed an annular neoplasm involving the sigmoid colon; the operation was unsuccessful and at autopsy there was revealed an annular mucinous carcinoma of the rectosigmoid, with extension to the perirectal tissues, and metastases to the retroperitoneal and mediastinal nodes, peritoneum, stomach, duodenum, ileum, heart, prostate, testis, gall bladder, liver and skin.

Case three is a 19-year-old white male, with diarrhoea thought to be due to highly-seasoned spaghetti eaten two weeks prior to entry. Rectal examination showed an annular constriction which could be palpated about six cm. above the anal orifice. No distinct ulceration was felt. Exploratory laparotomy with colostomy was done. Inoperable malignant growth involving the rectum and infiltrating the entire pelvis was found.

In his discussion, Ross states that relative rarity of cancer prior to the so-called "cancer age", appears still to be a definite factor in preventing the early correct diagnosis of such lesions. This reluctance to make a diagnosis of cancer because of the youth of the patient was responsible in the first of the three cases here reported, for the rectal symptoms being attributed to tuberculous stenosis; and in the third case it led to an initial diagnosis of ulcerative colitis. Ross further emphasizes a most valuable point, that each of these growths was readily palpable on simple digital-rectal examination, and that no special or complex laboratory procedure was needed to establish a firm clinical suspicion of the nature of the malady.

His four conclusions are as follows:

1. Carcinoma of the rectum is not strictly a disease of old age, two to four per cent occurring in patients under thirty.
2. There is no striking variation in the symptomatology of this disease with the patient's age.
3. Carcinomata of the rectum arising in youth are apparently more malignant than those of the later decades of life.
4. The majority of rectal carcinomata can be diagnosed by simple digital-rectal examination.

E. H. Gaither.

CARTY, JOHN R.; WEINTRAUB, SYDNEY, AND FELTER, ROBERT K.

An X-ray Study of the Post-Operative Stomach. Radiology, 22:191-196, 1934.

A careful clinical and roentgen study was made of 144 cases of peptic ulcer which had been treated surgically. The cases with satisfactory results all showed the stomach much smaller, placed higher and more laterally, with reduced peristaltic activity, lessened mobility, and a much more rapid emptying time. Rapid emptying of the stomach is deemed desirable and in none of the cases did untoward symptoms, such as diarrhea, result. In line with this, posterior gastroenterostomies with large openings placed near the pylorus were most consistently satisfactory.

Poor clinical results were noted in cases in which there had not been a considerable diminution in the size of the stomach, poor drainage being due to one or more of the following causes: the stoma was too small, the stoma was poorly placed, the proximal loop of the anastomosis was too long, the distal loop was kinked at the mesocolon. Emphasis is placed upon making a liberally large opening when operating upon a dilated, obstructed stomach to avoid shrinkage in the stoma as the stomach returns to normal size. A long proximal loop is apt to hinder drainage and establish a vicious cycle. In cases in which severe hemorrhage occurred a considerable time after operation, there being no signs of a recurrent ulcer, the authors found that either the stoma was too small or that the distal loop was obstructed, and offer as explanation the formation of varices at the stoma.

Roentgenologically, poor results are divided into: 1. Those with a disturbance of the mechanical factors, overly large stomach, poor emptying, hyperperistalsia, and poor placement of the stoma. 2. The cases which developed marginal ulcers, formed new ulcers elsewhere, reactivated the original ulcers or developed gastric hemorrhages. Although not relating as causal necessarily, poor mechanical function often was noted in this second group. The authors note a peculiar spasm of the proximal loop in marginal ulcers, and raise the question of its diagnostic significance.

X-ray examination of the post-operative stomach is a vital part of the follow-up study, as there is a definite correlation between the roentgenographic findings and the clinical results, which should lead to a fairly accurate prognostication, from the roentgen study, of good or poor clinical results. Systematic co-operation with the surgeon in this type of analysis should improve the results from gastric surgery by its more satisfactory elucidation of the physiology of the stomach which has been subjected to operation. James T. Case, Chicago, Ill.

BLOOM, DAVID.

Strictures of the Rectum in Lympho-granuloma Inguinale. S. G. and O., 58-5-827 (May, 1934).

He reports seven cases of lympho-granuloma inguinale and concludes: A review of the literature of "esthiomene" and "syphilome ano-rectal" on the one hand and of "benign rectal strictures" on the other, showed a remarkable resemblance in the confusion regarding their etiology. Most, if not all of these conditions, are identical and are due to the virus of lympho-granuloma inguinale. A routine Frei test should be made in benign stricture cases. Clement L. Martin.

Sectional Index for Volume One

SECTION I—CLINICAL MEDICINE

Amebiasis and Amebic Dysentery, *Charles F. Craig*.. 4
Amebic Dysentery in Chicago, *Herman N. Bundesen*.. 9
Certain Latent and Atypical Types of Amebiasis, *Philip W. Brown*..... 10
Migraine, and Allergic Phenomenon, *Albert F. R. Andresen* 14
Diagnosis and Management of Gall Tract, particularly Gall Bladder, Disease, *B. B. Vincent Lyon*.. 18
Gastric Ulcers Associated with Cinchophen Poisoning, *Leon Bloch* and *David H. Rosenberg*..... 29
Obstruction of the Upper Portion of the Small Intestine, *Andrew B. Rivers* and *Norman W. Thiessen* 92
The Broadening Conception of Regional Ileitis, *Burrill B. Crohn*..... 97
Food Allergy in its Relation to Gastrointestinal Disorders, *Julius Friedenwald* and *Samuel Morrison* 100
Report of an Instance of Suppurative Cholango-Hepatitis with Obstructive Jaundice, *B. B. Vincent Lyon, Damon B. Pfeiffer* and *John Eiman*.. 104
Observations upon Amebiasis, *Virgil E. Simpson*.... 109
Jaundice with Ascites, *William Fitch Cheney*..... 113
Chronic Ulcerative Enteritis, *Philip Corr* and *William C. Boeck*..... 161
Gastric Secretion following Irradiation of the Exposed Stomach and Upper Abdominal Viscera by Roentgen Rays, *Albert M. Snell* and *Jesse L. Bollman*..... 164
Single Gastric Polyp—Report of an Instance, *Martin G. Vorhaus* and *Arthur E. T. Rogers*..... 169
Recurrent "Hiatus Hernia" Syndrome of Von Bergmann, *Felix Cunha*..... 170
The Results of Treatment, Medical and Surgical, in Gall Bladder Disease, from a Clinician's Viewpoint, *Thomas R. Brown*..... 221
Late Manifestations of Amebiasis, *R. W. Mendelson*.. 228
Complement Fixation Test for Amebiasis (Preliminary Report), *Emil Weiss* and *Lloyd Arnold*.. 231
Lambliasis Simulating Cholecystitis—Report of Two Instances, *Meyer Golob*..... 233
Brilliant Blue F.C.F., a New Dye for Diagnostic Gastrointestinal Studies, *Arthur C. Taylor*..... 239
The Occurrence of a Pernicious Anemia Syndrome in the Presence of Normal Gastric Acidity—Report of an Instance, *A. L. Levin*..... 240
History of Gall Bladder Disease—Resume of Symptoms, *Martin E. Rehfuss*..... 289
A Practical Etiological, Pathological and Clinical Consideration of Intestinal Ulceration, *Joseph Felsen* 297
Insanity Equivalents and the Gastroenterologists, *Walter C. Alvarez*..... 305
Intravenous Galactose Liver Function Test (Preliminary Report), *I. R. Jankelson* and *H. H. Lerner* 310
Unusual Clinical Syndromes Associated with Stone in the Common Bile Duct, *Albert M. Snell* and *Mandred W. Comfort*..... 312
Commensal and Parasitic Entameba Histolytica Infestation, *Lloyd Arnold*..... 351
Treatment of Patients with Foreign Bodies in the Esophagus or Stomach, *Porter P. Vinson* and *Karl Deissler*..... 357
A New Aspect of Migraine and Certain Related Conditions, *Eugene Foldes*..... 359
Chronic Inflammatory Lesions of the Small Intestine (Regional Enteritis), *Philip W. Brown, J. Arnold Bargen* and *Harry M. Weber*..... 426
Cinchophen Poisoning, *Leon Bloch* and *David H. Rosenberg* 433
Pancreatitis, *V. C. Rowland*..... 441
Pathogenic Protozoa in the United States, *Robert Hegner* 456
A Report of the Committee "On a Survey of the Enzyme Tests", *A. H. Aaron, H. L. Bockus* and *A. C. Ivy*..... 462
The Importance to the Gastroenterologist of Inheritance in Disease, *Madge Thurlow Macklin*... 480
Diagnosis and Treatment of Amebiasis, *Sidney Simon* 486
Studies on the Alteration of Function in Biliary Tract Disease, *I. S. Ravdin*..... 496
Diseases of the Portal Vein, *James F. Weir* and *Donald C. Beaver*..... 498
The Clinical Use of Tests of Hepatic Function, *Carle H. Greene* and *Howard F. Shattuck*..... 505
A Histological Study of the Liver in Patients Affected with Peptic Ulcer, *Maurice A. Schnitker* and *George M. Hass*..... 537
The Effects of Dessiccated Hog's Stomach in Achlorhydria, *Leon Schiff* and *Toba Tahl*..... 543
The Specificity of the Complement Fixation Test for Amebiasis, *Emil Weiss* and *Lloyd Arnold*.... 548
Some Observations upon the Reciprocal Relationship between Gastrointestinal and Female Pelvic Disturbances, *Julius Friedenwald* and *Samuel Morrison*..... 609
Discussion and Appraisal of some Functional Disturbances of the Digestive Tract, *H. F. Kramer*.. 614
Gastrointestinal Studies—V.—Gastric Juice in Anemias Other than Pernicious Anemia, *Paul J. Fouts, O. M. Helmer* and *L. G. Zerfas*..... 667
The Influence of Mucilaginous Substances on the Emptying of the Stomach, *H. Necheles, H. I. Sapoznik, R. Arens*, and *Jacob Meyer*..... 684
Studies on the Gastric Hunger Mechanism, *Ira A. Manville* and *Eldon G. Chuinard*..... 688
Carcinoma of the Colon, *Charles W. Heald*..... 693
Notes on the Diagnosis and Prognosis in Gastric Ulcer: A Clinical Study of 500 Consecutive, Operatively Demonstrated Cases, *Frank Smithies* 697
An Unusual Right Diaphragmatic Hernia, *William C. Boeck* and *Wells C. Cook*..... 705
Diverticula of the Jejunum, *Jerome S. Levy* and *A. De Groat*..... 708
"Okrin" as an Adjuvant in the Treatment of Peptic Ulcer, *Arthur J. Atkinson*..... 718
The Problem of Infection in Gall Bladder Disease with a Report on the Experimental Production of Cholecystitis, *Martin E. Rehfuss* and *Guy M. Nelson* 759
Intestinal Giardiasis in New England with Notes on its Pathogenicity and Symptomatology, *Lee MacPhee* and *Burnham S. Walker*..... 768
Functional and Nervous Disorders of the Stomach and Alimentary Tract, *Burrill B. Crohn*..... 773
One Hundred and Sixty-Nine Studies of the Gastric Secretion During the Night, *Asher Winkelstein* 778
Clinical Notes Concerning Distal Ileitis as a Manifestation of Bacillary Dysentery, *Joseph Felsen* 782
Anemia Following Operations on the Stomach, *Howard R. Hartman* and *George B. Eusterman*.. 829

The Results of Fat Tolerance Tests and Blood Sugar Estimations Performed on Patients Affected with Peptic Ulcer. With a Discussion of Factors Possible in the Etiology of Peptic Ulcer, *Maurice A. Schnitker* and *E. S. Emery, Jr.*..... 834

An Instance of Gelatinous Carcinoma of the Duodenum, *J. Allen Wilson* and *John F. Noble*..... 840

SECTION II—EXPERIMENTAL PHYSIOLOGY

Sympathetic Secretory Innervation of the Gastric Mucosa, *Stewart G. Baxter*..... 36

Role of the Sympathetic Nervous System in Gastric Secretion, *Stewart G. Baxter*..... 40

The Relation of Gastrectomy to Anemia, *A. C. Ivy, O. Richter, A. F. Meyer* and *H. Greengard*..... 116

Gastrointestinal Studies: IV. The Relation of pH to the Pepsin and Rennin Content of the Gastric Juice, *O. M. Helmer, Paul J. Fouts* and *L. G. Zerfas*..... 120

An Investigation Concerning Certain Substances Reported to Affect the Motility of the Gall Bladder, *W. L. Voegtlin* and *A. C. Ivy*..... 174

The Antipeptic Influence of Gastric Mucin, *Earl A. Zaus* and *Leonard S. Fosdick*..... 177

The Influence of the Pylorus upon the Regulation of the Acidity of the Gastric Secretion, *William Walsh Lermann* and *Lyle M. Nelson*..... 245

The Composition of Pure Gastric Juice, *Franklin Hollander*..... 319

Recent Investigations Permitting a New Interpretation of the Results of the Conventional Titration of Gastric Juice, *Lay Martin*..... 330

Dissociation of the Functional Properties of the Gastric Glands Under the Influence of Fat, *Armine Alley, David W. MacKenzie* and *D. R. Webster*..... 333

A Further Proof that the Gall Bladder Evacuates via the Cystic Duct, *W. L. Voegtlin, H. Greengard* and *A. C. Ivy*..... 371

Studies on Gastric Motility Under Low Oxygen Pressures, *Edward J. Van Liere*..... 373

A Study of the Absorption of Dextrose and Water from Chronic Isolated Loops of the Colon, *Philip H. Moore* and *G. E. Burget*..... 376

Natural Chemical Factors Governing Gastric Motility, *J. P. Quigley*..... 425

A Resume of the Newer Physiology of the Pancreas, *Arthur C. Clasen*..... 445

An Experimental Study of the Lower End of the Esophagus, *Maurice Feldman* and *Samuel Morrison*..... 471

The Effects of Gastric Secretion in Dogs of Various Food Substances Employed in the Treatment of Gastric Ulcer, *Armine Alley*..... 555

A Note on the Role of Achlorhydria in the Etiology of Subacute Combined Degeneration of the Spinal Cord, *A. C. Ivy, F. P. Cuthbert* and *A. Weil*..... 560

Comparison of Methods for the Quantitative Estimation of Diastase in Duodenal Fluid, *C. R. Schmidt, H. Greengard* and *A. C. Ivy*..... 618

The "Chemical" Phase of Gastric Secretion and Its Regulation, *H. P. Babkin*..... 715

Accessible Closed Loops of the Small Intestine and the Colon, *G. E. Burget*..... 722

The Bacteriocidal Power of the Stomach and Some Factors which Influence It, *Arthur Hanszen*.... 725

The Inhibitory Effect of Histamine on Gastric Secretion, *Armine Alley*..... 787

The Applied Physiology of the Gastrointestinal Innervation, *A. C. Ivy*..... 845

The Effect of Mechanical Stimulation of the Duodenum, Colon, and the Stomach on the Cerebral Circulation and Intracranial Pressure, *John Vandolah* and *Lathan A. Crandall*..... 853

SECTION III—NUTRITION

Nutrition in Health and Disease, *Clifford J. Barborka*..... 44

Lower Fat Diet in Diabetes, *Joseph H. Barach*..... 124

Estimation of the State of Hydration of the Body by the Amount of Water Available for the Solution of Sodium Thiocyanate, *Lathan A. Crandall* and *Milford X. Anderson*..... 126

The Dietary Phases of Pernicious Anemia, *Beaumont S. Cornell*..... 132

Mortality in Diabetic Children, *Henry J. John*..... 180

The Effect on the Gastric Juice Secretion of Various Cooked Preparations of Haddock (Melanogrammus Aeglefinus) and of Lobster (Homarus Americanus), *A. Alley*..... 182

A Study of Obesity in an Outpatient Clinic, *Edgar C. Beck* and *Roger S. Hubbard*..... 250

The Incidence and Significance of Disease of the Gall Bladder and Liver in Pernicious Anemia, *Frank H. Bethel* and *Bernard D. Harrington*... 256

Some Observations on Food Allergy, *Warren T. Vaughan*..... 384

Revised "Elimination Diets" for the Diagnosis and Treatment of Food Allergy, *Albert H. Rowe*..... 387

The Role of the Gastrointestinal Tract in Conditioning Deficiency Disease, *Maurice B. Strauss*..... 426

Diabetes Mellitus, its Physiological Essence and Rational Treatment, *W. N. Boldyreff*..... 453

Clinical Types of Hyperinsulinism, *Seale Harris*..... 562

Diabetic Coma in Children, *Henry J. John*..... 569

The Complete Treatment of Pernicious Anemia, *Russell L. Haden*..... 623

A Convenient Method of Establishing Diet and Insulin Therapy in Diabetes, *Sister Mary Edwina*.. 728

Studies in Food Allergy (Preliminary Report), *A. W. Oelgoetz, P. A. Oelgoetz* and *J. Wittekind*... 730

Vitamin A as a Prophylactic Against the Common Cold in Groups of School Children, *Esther M. Tress*..... 795

Growth of Diabetic Children, *Henry J. John*..... 855

The Nutritional and Digestive System Aspects of Pernicious Anemia, *L. G. Zerfas* and *Beaumont S. Cornell*, Part I..... 857

SECTION IV—ROENTGENOLOGY

Cholecystocolic Fistula with X-Ray Demonstration, *Martin G. Vorhaus* and *Arthur E. T. Rogers*.... 133

Why Peptic Ulcers are Missed on X-Ray Examination, *Wm. H. Stewart* and *H. Earl Illick*..... 52

X-Ray's Contribution to the Diagnosis of the "Acute Abdomen", *Wm. H. Stewart* and *H. Earl Illick*.. 185

Factors of Error in Roentgenological Distinction Between the Normal and the Diseased Stomach and Duodenum, *B. R. Kirklin*..... 260

Intensified Oral Cholecystography (Preliminary Report), *Wm. H. Stewart* and *H. Earl Illick*..... 337

A Bacteriological, Roentgenological and Clinical Study of Ulcerative Colitis, *Thomas T. Mackie*... 466

The Niche as a Criterion in the Healing of Peptic Ulcer, *Jacob Buckstein*..... 516

X-Ray Diagnosis of Activity and Cure of Duodenal Ulcer, *Alice Ettinger* and *W. E. Davis*..... 579

Roentgenographic Differentiation between Diverticulitis and Cancer of the Sigmoid, *Wm. H. Stewart* and *H. Earl Illick*..... 738

The Differentiation of Confusing Shadows in Cholecystography, *Morris A. Hershenson*..... 799

SECTION V—THERAPEUTICS

Treatment of Amebic Dysentery, *Horace W. Soper*.. 58

Insulin in the Treatment of Peptic Ulcer, *Clement R. Jones*..... 135

Chronic Ulcerative Colitis: Trends in its Present-Day Management, *J. Arnold Bargen*..... 190

Treatment of Peptic Ulcer with Bacterial Vaccines (Foreign Protein), *David J. Sandweiss* and *S. G. Meyers* 338
The Management of Chronic Spastic Constipation, *Harvey G. Beck* 393
The Treatment of Pernicious Anemia, *S. M. Goldhamer* and *F. H. Bethell* 398
The Significance of Alkalosis in the Treatment of Peptic Ulcer, *S. Allen Wilkinson* and *Sara M. Jordan* 509
Aluminum Hydroxide in the Treatment of Peptic Ulcer, *I. H. Einsel, W. Lloyd Adams* and *Victor Myers* 513
The Treatment of Peptic Ulcer Based on 1435 Cases, *E. S. Emery* 520
A Rationale for the Treatment of Peptic Ulcer, *Andrew B. Rivers* and *Thomas J. Dry* 522
A New Type of Serum for the Treatment of Non-Specific Ulcerative Colitis, *Gregory Schwartzman* and *Asher Winkelstein* 582
Treatment of Functional Vomiting, *C. H. Drenckhahn* and *D. L. Wilbur* 635
The Treatment of Massive Gastroduodenal Hemorrhage, *Frank Smithies* 803
Medical Aspects of Peptic Ulcer with Special Reference to Diagnosis and Treatment, *Arthur F. Chase* 866

SECTION VI—ABDOMINAL SURGERY

Primary Carcinoma of Liver in Infancy, *Ralph A. Kordenat* 60
Two Specimens of Gastric and Duodenal Ulcers Anatomically Cured by Surgery, *L. Blagdon* and *L. C. Simard* 130
Diverticulosis and Diverticulitis of the Small Intestine, *Irvin Abell* 193
The Congenital Pericolic Membrane Syndrome, Often Misnamed Chronic Appendicitis (A Preliminary Report of Observations), *W. H. Baermann* 196
Acute Liver Degeneration: Treatment by Cholecystogastrostomy with Discussion of the Clinical, Pathological and Physiological Accompaniments, *Chas. Gordon Heyd* 203
Conservative Surgical Treatment of Ulcer of the Stomach and Duodenum, *E. Starr Judd* and *George W. Waldron* 262
An Analysis of the Results of Biliary Tract Surgery, *John T. Howard* 270
The Treatment of Carcinoma of the Colon, *W. Wayne Babcock* 342
The Uncommon Tumors of the Large Intestine, *J. Arnold Bargen* and *Claude F. Dixon* 400
Some Principles in the Treatment of Septic Conditions Following Abdominal Diseases, *James N. Coombs* 404
Lowering the Mortality from Appendicitis, *J. Russell Verbrycke* 477
The Incidence of Gastrojejunal Ulcer Following Gastroenterostomy, *J. William Hinton* and *Reynold E. Church* 526
Carcinoma of the Colon, *Roscoe R. Graham* 584
The Relation of Anemia to Surgical Diseases of the Gall Bladder, *Ralph A. Kordenat* 638
"Silent" Carcinomas of the Large Intestine, *E. Lee Strohl* and *J. Arnold Bargen* 808
Portal Cirrhosis: The Combined Medical and Surgical Management, *Howard A. Rusk* and *Harold G. Newman* 810
Diseases of the Pancreas, Especially Acute Pancreatitis and its Treatment, *John Douglas* 871

SECTION VII—SURGERY OF THE LOWER COLON AND OF THE RECTUM

Unusual Problems in Plastic Surgery of the Colon, *Jerome M. Lynch* and *Vincent Hurley* 66
Multiple Fissures of the Anus in a Case of Tertiary Syphilis, *Louis A. Buie* and *Winfield L. Butsch* .. 69
Tuberculous Ulceration of the Rectum and Sigmoid, *Clement L. Martin* 70
Diagnostic Criteria of Rectal Cancer, *Curtice Rosser* 141
Anal Fissure and its Management, *Clement L. Martin* 144
Diverticulitis of the Colon (with Abscess Formation), Initiated by Trauma from an Enema Tip, *Jerome M. Lynch* and *Max P. Cowett* 207
Treatment of Hemorrhoids, *Jerome M. Lynch* and *Vincent Hurley* 409
Peri-Rectal Streptococcal Cellulitis—Report of a Case, *Herbert T. Hayes* 413
High Rectal Pain—An Analysis of 100 Cases, *Louis A. Buie* and *John C. M. Brust* 591
Malignancies of the Colon with Special Reference to the Rectal Zone, *John F. Erdmann* 881

SECTION VIII—EDITORIAL

Foreword, *Frank Smithies* 72
Board of Gastroenterology, *Albert F. R. Andresen* .. 72
Endamebiasis in the United States, *Frank Smithies* .. 73
Familial Incidence of Peptic Ulcer, *Frank Smithies* .. 76
Medical Therapy to Combat Amebiasis, *Frank Smithies* 147
Gastric Acidity and Associated Gastric Disease, *Frank Smithies* 148
Higher Education and the "Sluggish System", *Frank Smithies* 209
The Prompt Dissemination of Medical Knowledge, *Frank Smithies* 274
Medicine: A Profession, Trade or Tent Show? *Frank Smithies* 275
The Controlled Circulation Racket, *Frank Smithies* .. 346
The Affiliation of the Journal with the American Gastroenterological Association, *B. B. Vincent Lyon* 415
The Journal, its Readers and the American Gastroenterological Association, *Frank Smithies* 415
American Board of Gastroenterology, *Albert F. R. Andresen* 595
The Need for Printing Reforms in Medical Journals, *Beaumont S. Cornell* 595
The Journal's New Department, "The Clinic", Frank *Smithies* 596
Shall We Have Stomach Specialists or Internists Certified as Gastroenterologists, *Frank Smithies* 646
Proposed Constitution and By-Laws of the American Board of Gastroenterology 649
Electro-Chemical Processes Underlying Gastric and Pancreatic Secretion, *Walter C. Alvarez* 743
Abstracts of Medical Literature, *Frank Smithies* 817
A Letter, *W. N. Boldyreff* 818
The "Graduate Fortnight", *Frank Smithies* 889
Experience with Blood Transfusion, *Walter C. Alvarez* 891
The Journal Enjoys its First Birthday, *Beaumont S. Cornell* 891

SECTION IX—BOOK REVIEWS

Diseases of the Digestive Tract by *Arthur L. Bloomfield.* Reviewed by *Beaumont S. Cornell* .. 77
Mystery, Magic and Medicine by *Howard W. Haggard.* Reviewed by *Frank Smithies* 77
The Great Doctors by *Henry E. Sigerist.* Reviewed by *Frank Smithies* 150
Food Allergy by *Albert H. Rowe.* Reviewed by *Beaumont S. Cornell* 151
Behaviour Patterns of the Alimentary Tract by *T. Wingate Todd.* Reviewed by *Beaumont S. Cornell* 152
Die Hormone by *Paul Trendelenburg* and *Otto Krayer.* Reviewed by *Henry J. John* 211

Modern Aspects of Gastroenterology by *M. A. Arafa*. Reviewed by *Martin G. Vorhaus*..... 211
Gastric Anacidity by *Arthur L. Bloomfield* and *W. Scott Polland*. Reviewed by *Oscar M. Helmer*, also by *Beaumont S. Cornell*..... 212
A New Approach to Dietetic Therapy in Epilepsy by *Eugene Foldes*. Reviewed by *Clifford J. Barborka* 214
Alimentacion by *Pedro Escudero*. Reviewed by *Howard F. Root*..... 214
Nutrition by *Graham Lusk*. Reviewed by *Frank Smithies* 277
The Vitamins in Health and Disease by *Barnett Sure*. Reviewed by *Beaumont S. Cornell*..... 279
Functional Disorders of the Large Intestine and Their Treatment by *Jacob Buckstein*. Reviewed by *Beaumont S. Cornell*..... 350
Physical Diagnosis by *Richard C. Cabot*. Reviewed by *Frank Smithies*..... 598
Die Pathologische-anatomischen Grundlagen der Chirurgie des Rektumkarzinoms by *Heinrich Westhues*. Reviewed by *Clement L. Martin*..... 745
Amebiasis and Amebic Dysentery by *Charles F. Craig*. Reviewed by *Thomas B. Magath*..... 819
Beitrag zur Kenntnis des Ileum Terminale Fixatum und Ileus Ilei Terminalis Fixati by *L. Peterson*. Reviewed by *W. C. Alvarez*..... 892

SECTION X—AFTER HOURS

The Goldheaded Cane, *Anonymous*.....80, 153, 280
The Evolution of Our Diet by *Samuel S. Altshuler* 215
Astrological Physick by *Clement L. Martin*..... 417
William Bodenhamer by *Simon B. Kleiner*..... 601
Jean Paul Marat, M.D., by *J. Duffy Hancock*..... 653
Academician I. P. Pavlov by *W. N. Boldyreff*..... 747
History of Gastroenterology by *Fielding H. Garrison* 893

SECTION XII—"THE CLINIC"

Impalement of the Rectum: Operation and Recovery, *Martin S. Kleckner*..... 604
Toxic Cirrhosis Due to Cincophen: Recovery, *Henry F. Kramer*..... 605
Rectosigmoid Cancer with Acute Gangrene of Pelvic Organs, *Charles E. Howard*..... 669
An Instance of Uncontrollable Vomiting: Recovery, *Frank Smithies*..... 671
Polyposis of Duodenum and Jejunum, *John M. Cassidy* and *Benjamin J. Macchia*..... 755
An Instance of Syphilis of the Stomach, *V. C. Rowland* and *E. E. Woldman*..... 822
An Unusual Instance of Primary Myosarcoma of the Stomach with Recovery Following Operation, *M. E. Gabor*, *M. Tufts* and *W. C. F. Witte*.. 825
High Rectal Pain Relieved by Elimination and also by "Test-free" Diets, *F. W. Bramigk*..... 899
Dystrophia Adiposogenitalis and its Related Disturbances, *C. Victor Richards*..... 900

Author Index for Volume One

A

Aaron, A. H..... 462
Abell, Irvin..... 193
Adams, W. Lloyd..... 513
Alley, Armine.....182, 333, 555, 787
Altshuler, Samuel S..... 215
Alvarez, Walter C.....305, 743, 892
Anderson, Milford X..... 126
Andresen, Albert F. R.....14, 72, 595
Arens, R..... 684
Arnold, Lloyd.....231, 351, 548
Atkinson, Arthur J..... 718

B

Babcock, W. Wayne..... 342
Babkin, B. P..... 715
Barach, Joseph H..... 124
Barborka, Clifford J.....44, 214
Bargen, J. Arnold.....190, 400, 426, 808
Baxter, Stewart G.....36, 40
Beaver, Donald C..... 498
Beck, Edgar C..... 250
Beck, Harvey G..... 393
Bethell, F. H.....256, 398
Blagdon, L..... 137
Bloch, Leon.....29, 433
Bochus, H. L..... 462
Boeck, Wm. C.....161, 705
Boldyreff, W. N.....453, 747, 818
Bollman, Jesse L. 164
Bramigk, F. W..... 899
Brown, Philip W.....10, 426
Brown, Thomas R..... 221
Brust, John C. M..... 591
Buckstein, Jacob..... 516
Buecrmann, W. H..... 196
Buie, Louis A.....69, 591
Bundesen, Herman N..... 9
Burget, G. E.....69, 376, 722

C

Cassidy, J. M..... 755
Chase, Arthur F..... 866
Cheney, Wm. F..... 113
Church, Reynold E..... 526
Chuinard, Eldon G..... 688
Clasen, Arthur C..... 445
Comfort, Manfred W..... 312
Cornell, Beaumont S.
.....77, 132, 151, 152, 212, 279, 350, 857
Cook, W. C..... 705
Coombs, James N..... 404
Corr, Philip..... 161
Cowett, Max P..... 207
Crandall, Lathan A.....126, 853
Craig, Chas. F..... 4
Crohn, Burrill B.....97, 773
Cunha, Felix..... 170
Cuthbert, F. P..... 560

D

Davis, W. E..... 579
DeGroat, A..... 708
Deissler, Karl..... 357
Dixon, Claude F..... 400
Douglas, John..... 871
Drenckhahn, C. H..... 635
Dry, Thomas J..... 522

E

Edwina, Sister Mary ... 728
Eimen, John ... 104
Einsel, I. H. ... 513
Emery, E. S., Jr. ... 520, 834
Erdmann, John F. ... 881
Ettinger, Alice ... 579
Eusterman, George B. ... 829

F

Feldman, M. ... 471
Felsen, Joseph ... 297, 782
Foldes, Eugene ... 359
Fosdick, L. S. ... 177
Fouts, Paul J. ... 120, 667
Friedenwald, Julius ... 100, 609

G

Gabor, M. E. ... 825
Garrison, Fielding H. ... 893
Goldhamer, S. M. ... 398
Golob, Meyer ... 233
Graham, Roscoe R. ... 584
Greene, Carle H. ... 505
Greengard, H. ... 116, 371, 618

H

Haden, Russell L. ... 628
Hancock, J. Duffy ... 653
Hanszen, Arthur ... 725
Harrington, Bernard D. ... 256
Harris, Seale ... 562
Hartman, Howard R. ... 829
Hass, George M. ... 537
Hages, Herbert T. ... 413
Heald, Chas. W. ... 693
Hegner, Robert ... 456
Helmer, O. M. ... 120, 212, 667
Hershenson, M. A. ... 799
Heyd, Chas. G. ... 203
Hinton, J. W. ... 526
Hollander, Franklin ... 319
Howard, Chas. E. ... 669
Howard, John T. ... 270
Hubbard, Roger S. ... 250
Hurley, Vincent ... 66, 409

I

Illick, H. Earl ... 52, 185, 337, 738
Ivy, A. C. ... 174, 371, 462, 560, 618, 845

J

Jankelson, I. R. ... 310
John, Henry J. ... 180, 211, 569, 855
Jones, Clement R. ... 135
Jordan, Sara M. ... 509
Judd, E. Starr ... 262

K

Kirklin, B. R. ... 260
Kleckner, M. S. ... 604
Kleiner, S. B. ... 60
Kordenat, Ralph A. ... 60, 638
Kramer, Henry F. ... 605, 614

L

Lermann, W. W. ... 245
Lerner, H. H. ... 310
Levin, A. L. ... 240
Levy, Jerome S. ... 708
Lynch, Jerome M. ... 66, 207, 409
Lyon, B. B. Vincent ... 18, 104, 415

M

Macchia, B. J. ... 755
MacKenzie, D. W. ... 333
Mackie, Thomas T. ... 466
Macklin, Madge T. ... 480
MacPhee, Lee ... 768
Magath, Thomas B. ... 819
Martin, Clement L. ... 70, 144, 417, 745
Martin, Lay ... 330
Mendelson, R. W. ... 228
Meyer, A. F. ... 116
Meyer, Jacob ... 684
Meyers, S. G. ... 338
Moore, Philip H. ... 376
Morrison, Samuel ... 100, 471, 608
Myers, Victor C. ... 513

N

Necheles, H. ... 684
Nelson, Guy M. ... 759
Nelson, L. M. ... 245
Newman, Harold G. ... 810
Noble, John F. ... 840

O

Oelgoetz, A. W. ... 730
Oelgoetz, P. A. ... 730

P

Pfeiffer, Damon B. ... 104

Q

Quigley, J. P. ... 425

R

Ravdin, I. S. ... 496
Rehfuss, Martin E. ... 289, 759
Richards, C. Victor ... 900
Rivers, Andrew B. ... 92, 522
Rogers, Arthur E. T. ... 133, 169
Root, Howard F. ... 214
Rosenberg, David H. ... 29, 433
Rosser, Curtice ... 141
Rowe, Albert H. ... 387
Rowland, V. C. ... 441
Rusk, Howard A. ... 810

S

Sandweiss, D. J. ... 338
Sapoznik, H. I. ... 684
Schiff, Leon ... 543
Schmidt, C. R. ... 618
Schnitker, N. A. ... 537, 834
Schwartzman, G. ... 582
Shattuck, Howard F. ... 505
Simon, Sidney ... 486
Smithies, Frank ... 72, 73, 76, 77, 147, 148, 150, 209, 247, 275, 277, 346, 415, 596, 598, 646, 671, 697, 803, 817, 889
Simard, L. C. ... 130
Simpson, Virgil E. ... 109
Snell, Albert M. ... 312
Soper, Horace W. ... 58
Stewart, Wm. H. ... 52, 185, 337, 738
Strauss, Maurice B. ... 426
Strohl, E. Lee ... 808

T

Tahl, Toba ... 543
Taylor, Arthur C. ... 239
Thiessen, Norman W. ... 92
Tress, Esther M. ... 795
Tufts M. ... 825

V

Vandolah, John ... 853
Van Liere, Edward J. ... 373
Vaughan, Warren T. ... 384
Verbrycke, J. Russell ... 477
Vinson, Porter P. ... 357
Voegtlin, W. L. ... 174, 371
Vorhaus, Martin G. ... 133, 169, 211

W

Waldron, George W. 262
Walker, Burnham S. 768
Weber, Harry M. 426
Webster, D. R. 333
Weil, A. 560
Weiss, Emil 231, 548
Wilbur, D. L. 635
Wilkinson, S. Allen 509
Wilson, J. Allen 840
Winkelstein, Asher 582, 778
Witte, W. C. F. 825
Wittekind, J. 730
Woldman, E. E. 822

Z

Zaus, Earl A. 177
Zerfas, L. G. 120, 667, 857

General Index for Volume One

Abdomen, acute 318
"acute", X-ray in diagnosis 186
Abscess, of liver 228, 589
liver, due to basteroides funduliformis 243
pulmonary, in amebiasis 229
subphrenic 405
tropical 31
Acetyl-B-Methylcholine 63
Acetylcholine (experimental) 175
Achalasia 773
Achlorhydria, hog's stomach in 543
and hyperinsulinism 563
in cord lesion 560
Achylia gastrica, new definition 123
Acid, hydrochloric (experimental) 175
mucoitin-sulphuric 561
oleic 21
Acidity, gastric after gastrectomy 123
gastric in various diseases 34
gastric and gastric disease 148
gastric and pylorus 245
gastric regulation of 123
Acidosis, in diabetes 181
Action, specific dynamic action 50
Acute liver degeneration 203
"Addisin" 118
Adenoma of pancreas 64
Adenomatosis coli 140
Adenomyoma of colon 402
recto-vaginal septum 593
Adhesions, post-operative 93
Adrenalin, in food allergy 102
Aerophagia 292
Affinity, elective 759
Albumin, egg (experimental) 178
Alcohol in gall bladder disease 296
Alcoholic neuritis, digestion and absorption in 431
Alimentary allergy 100
Alkalemia 93
Alkalosis, in treatment of peptic ulcer 509
Allergy, food 100, 151, 730
in migraine 16
in ulcerative colitis 468
Aluminum hydroxide in treatment of peptic ulcer 513
Ameba carriers 354
Amebiasis 4, 819
atypical 10
complement fixation test for 5, 231, 548
diagnosis of 31, 299
diagnosis and treatment 487
in New Jersey 31
in prisoners 244, 318
late manifestations 228
medicinal treatment 147
observations upon 109
in private practice 33
nursing in 32
pathology of 5
stool culture 112
treatment of 13, 300
Amebic dysentery 4
blood picture in 5
diagnosis 5
in Chicago 9
incubation period of 5
treatment of 58
Amebic infection in ulcerative enteritis 161
Ampulla, of Vater 20
Anemia, achylic 140
after gastric operation 829
gastric juice in 677
hypochromic 116
in endocrine dysfunction 683
in gall bladder disease 638
in gastrectomy 116
hemolytic 683
idiopathic hypochromic 678
in pellagra 680
in pregnancy 683
pernicious, after stomach operations 829
pernicious, dietary phases 131
pernicious, experimental 116
pernicious, treatment 184
refractory to treatment 681
Angioma of colon 402
Anoxemia, effect on stomach 248
Anorexia nervosa 773
Antipeptic influence of mucin 177
Apparatus, special X-ray 53
Appendicitis 64, 813
acute 272
chronic 196
mechanics of 272
mortality in 477, 815
"so-called 102
Appendico-gastric 852
Appendix 272
Arsenic, in amebiasis 13
in colitis 191
Arsphenamine, in amebiasis 31
Arthritis 634
chronic 438
in gall bladder disease 291
nutrition in 370
Aspirates, biliary drainage 21
Asthenia, neurocirculatory and hyperinsulinism 564
Atrophy, of liver, acute 30
yellow, subacute 314
Atropine (experimental) 175
sulphate 21
valerianate 21
Aura in migraine 16

Bacillus coli 222
B. Coli in pernicious anemia 256

B. Welchii, in pernicious anemia 256
Bacteria, in pernicious anemia 863
Bacterial vaccines in peptic ulcer 338
Bacteroides funduliformis 243
Balantidium coli 457
Balloon sign 197
Banana diet 578
Band, ileo-pelvic of Treves and Lane 197
Behavior patterns of GI tract 152
Belching 101
Beriberi, from dieting 578
Bile duct obstruction 272
Bile, in peptic ulcer 835
white 22
Biliary tract, disease 496
physiology of 794
Bilirubin, in obstruction 93
in pernicious anemia 257
Biopsy, in rectal cancer 143
Bleeding from stomach 370
Blood diastase, function of 447
Brilliant blue, F. C. F. 239

Calcium chloride (experimental) 175
Calcium, in colitis 191
in food allergy 102
Cancer, colonic 34
of colon 63, 584, 693, 818
gastric 828
gelatinous 840
primary 244
rectal 141
recto-sigmoid 669
of rectum 63
stomach in young 242
of stomach 588
Cankers 101
Carbasone, in amebiasis 31, 32
Carbazone, rectally 583
Carbohydrates, influence on gastric motility 425
Carcinoid, iliac 590
Carcinoma, coli 140
of colon 584, 888
of colon, treatment of 342
of liver 553
of ovary and rectum 146
of pancreas 114
primary of liver 60
rectal 141
silent 808
of stomach 140, 214
Cardiac disease in gall bladder disease 222
Casts, intra-hepatic duct 104
extra-hepatic duct 104
pancreatic duct 107
Cellulitis, peri-rectal streptococcus 413
Cerebral, of adiposity 250
Cerebrum, circulation in 853
Chlorides, loss in obstruction of intestine 92
Children, diabetic mortality in 180
Chilomastix mesnili 457
Cholesteatoma of colon 402
Cholango-hepatitis 104
Cholecystectomy in giardiasis 771
Cholecystitis 19, 369, 785
calculous 760
chronic 23
experimental 759
and hyperinsulinism 563
simple catarrhal 20
suppurative 22
Cholecysto-gastric 852
Cholecystogastrostomy 203
Cholecystography 22
confusing shadows in 799
intensified oral 337
Cholecystokinin 176
Choleresis 115
Cholesterine, formation of typhoid fever 222
Cholesterol, bile plasma 248
diathesis 290
dinitrophenol and urobilinuria 786
effect of adrenal 828
of food 798
Cholesterosis of gall bladder 19, 21
Choline, effects of 248
Chondroitin sulphuric acid action on pepsin 178
Chordoblastoma of colon 403
Chronic cicatrizing 161
Cinchophen, in gastric ulcer 29
poisoning 433
Circulatory failure, acute 248
Cirrhosis, cincophen 605
hepatic 315
of liver 554, 222
causing gall bladder disease 222
portal 810
toxic 844
Clysma, barium 188
nutrient 805
Coccigodynia 592
Codeine, in colitis 191
Colic, biliary 189
Colitis, chronic ulcerative 190
relapse in 244
Colitis, mucous 101
non-specific ulcerative 582
ulcerative 70
ulcerative idiopathic 302
Colon, accessible closed loops of 722
cancer of 693
carcinoma of 584
disease associated with gall bladder disease 291
in arthritis 370
malignancies of 881
physiology of 123
spastic 70
surgery of 66
Colonic irrigation 397
Colopathy, atonic and hypertonic 785
Colostomy 879
Coma, diabetic, mechanism of 576
in diabetic children 181, 569
Complement fixation test, amebiasis 231, 548
Congenital bands 93
Constipation 101
atonic 394
in migraine 16
spastic 393
Convulsions and hyperinsulinism 566
Cramping 101
Crisis, Dietl's 23
tabetic rectal 592
Crypts, anal 821
anal, histopathology of 146
Cystic duct 371
obstruction 19
Cystine (experimental) 175
Cystocele 593
Cysts, hydatid 22
of cecum 402

Deficiency disease, gastrointestinal tract in 431
Deficiency, in ulcerative colitis 467
Degeneration, acute liver 203
oleaginous 105
subacute combined of spinal cord 560
Dehydration, in intestinal obstruction 92
Dermoids of colon 402
Desensitization to foods 389
Dextrose, absorption 376
absorption by rectum 192

Diabetes, and gall bladder disease 224
and hyperthyroidism 864
in children 190, 855
insulin in 728
lower fat diet 124
mellitus 48
physiology of 453
treatment of 453
Diabetic coma in children 569
Diagnosis, amebiasis 487
of food allergy 388
of pancreatic disease 446
of rectal cancer 141
Diaphragm, milking effect on esophagus 473
pinch-cock effect 475
Diarrhea 101, 298, 342
in lambliasis 235
in migraine 16
in terminal ileitis 427
Diastase, blood 447
quantitative estimation of 618
Diathesis, cholesterol 290
Dibothriocephalis latus 318
Dientameba fragilis 4, 457
Diet, average adult 47
banana 578
elimination 102
essential requirements 46
fat-full 21
for adiposity 252
in chronic ulcerative colitis 191
in diabetes 728
in disease 47
Jarotsky's 555
lower fat 124
Sippy's 555
Smithies' 558
"test-free" 899
trial 102
Dietotherapy in migraine 365
Dilation, digital in fissure 144
Dilitation of stomach 408
Diothane, in anal surgery 888
Diplostreptococcus, of chronic ulcerative colitis 190
Disease, deficiency 48
functional 614
Hunner's 23
inheritance in 480
of biliary tract 892
pituitary 797
requiring diets 47
Disorder, functional 773
Disturbance, functional 614
Diverticula, colon 272
duodenum 272, 553
esophagus 272
of jejunum 708
Diverticulitis, of colon 207
small intestine 193
Diverticulum, Meckel's 588
pharyngo-oesophageal 590
ruptured 188
Dizziness, in adiposity 251
in gall bladder disease 295
Dose, of insulin 728
Drainage, duodenal-tube 104
(medical) of gall bladder 224
Drugs, anti-amebic 583
Duct casts 104
Duodenal ulcer and hyperinsulinism 563
Duodenitis 223, 802
Duodeno-ileo-colic 851
Duodenum, cancer of 840
inversion 369
obstruction of 92
redundant 34, 115, 173
stasis of 92
X-ray of 260
Dye FCF 239
Dysentery, amebic 819
bacillary 244, 318, 782
bacillary, diagnosis of 301
bacillary, treatment of 301
mixed type 115
Dysfunction, endocrine 610
of gall bladder 20
of extra-hepatic ducts 20
Dysinsulinism 565
Dyskinesia, biliary 20, 785
Dysphagia 171
Dyspnea, in adiposity 251
Dystrophia, adiposogenitalis 900

Egg albumin (experimental) 178
Elimination diets 387
Emetin 13
Empyema of gall bladder 19, 22
Endameba, coli 4, 457
gingivalis 457
histolytica 4, 297, 457
cultivation of 32
demonstration of 5
discovery of 4
in colitis 243
pathogenicity test 32
Puerto Rican strain of 32
in gall bladder 23
Endamebiasis in U. S. A. 73
Endocrine disease in adiposity 253
Endocrinology 634
Endolimax nana 4
Endothelioma of colon 403
Entameba commensal 351
Enteritis, chronic ulcerative 161
in giardiasis 769
regional 426
tuberculous 70
Enteromonas hominis 457
Enzyme diagnosis of pancreatic disease 447
Eosinophilia in lambliasis 235
Ephedrine (experimental) 174
Epidemics of amebic dysentery 5
Epinephrine (experimental) 175
Epithelioma, anal 141
Esophagus, congenitally short 554
Esophagus, experimental study of 471
tumors of 828
X-ray method 370
Etiology of gall bladder disease 18
Exogenous, of adiposity 250
Exudate, "beef broth" 874

Factor, intrinsic gastric 116
Fat, influence on gastric glands 333
influence on gastric motility 425
Fecolith 197
Feedings, sham 788
Felly's syndrome 244
Female, pelvic disease 609
Fibroma, of colon 401
Fish tapeworm infestation 318
Fissure, anal 69, 144
Fistula, acute duodenal 815
anal, 2-stage operation 146
cholecystocolic 133
duodenal 272
gastrocolica-jejunalis 134
in-ano 590
intestinal 97, 583, 880
pancreatic 784
Flora, biliary 179
intestinal, in tropics 318
Fluorine, effects of 259

Fluoroscopy in peptic ulcer ... 52
Focal infection in migraine ... 16
Foci, infective ... 763
Follow-up management of gall bladder cases ... 28
Food allergy ... 100, 151, 384, 387
Food handlers and amebiasis ... 33
Foods, effect on gastric secretion ... 555
protective ... 44
Foreign bodies in esophagus and stomach ... 357
Foreign protein in peptic ulcer ... 338
Functional changes, in biliary tract disease ... 496
Functional disorder of stomach ... 773

Galactose, intravenous ... 310
Gall bladder ... 371
acute ... 188
and giardiasis ... 769
disease ... 18
disease, anemia in ... 638
acute ... 289
chronic ... 289
experimental ... 759
history in ... 289
indigestion in ... 289
latent ... 292
pernicious anemia in ... 256
infection ... 759
motility ... 174
motor mechanism of ... 222
"strawberry" ... 21
stoneless ... 880
Gall stones ... 290
cholesterol ... 272
Gall stone disease ... 20
Gall tract disease ... 18
Gangrene, pelvic ... 669
Gastrectomy ... 271
and achylic anemia ... 140
relation to anemia ... 116
Gastric acidity, after pyloric closure ... 179
and pylorus ... 245
normal in pernicious anemia ... 240
Gastric glands, influenced by fat ... 333
Gastric juice, composition ... 319
Pawlow theory of ... 329
pH of ... 120
titration of ... 330
Gastric motility ... 373
fats in ... 425
chemical factors in ... 425
Gastric secretion, following irradiation ... 164
nocturnal ... 778
second phase ... 248
with haddock ... 181
with lobster ... 181
Gastric studies on man ... 383
Gastric tumors ... 581
benign ... 140
Gastric ulcer, in cinchophen poisoning ... 433
Gastritis ... 115
chronic follicular ... 192
Gastroenterostomy and achylic anemia ... 140
ulcer following ... 526, 590
Gastro-globulin ... 330
Gastro-jejunal ulcer ... 526
Gastrointestinal, disorders due to allergy ... 100
manifestations ... 243
tract in deficiency disease ... 392
Gavano, in amebiasis ... 32
Gelatinaise ... 248
Gentian violet, in colitis ... 191
Giardia intestinalis in gall bladder ... 23
lamblia ... 457
Giardiasis ... 768
Glands, inflammatory causing duodenal obstruction ... 93
salivary ... 845
Glioma of colon ... 403
Gout, experimental ... 737
Growth, diabetic children ... 855
Guanidine (experimental) ... 175

Haddock, effect on gastric juice ... 181
Headaches, in gall bladder disease ... 290
Heart, in gall bladder disease ... 290, 291
Heaviness, epigastric ... 101
Hemorrhoids, treatment of ... 409
Hemicrania ... 15
Hemochromatosis endocriopathies ... 243
Hemorrhage, gastro-duodenal ... 803
intra-abdominal ... 189
Hepatectomy ... 854
Hepatic function tests ... 505
Hepatoma ... 61
Heredity, in functional disease ... 774
Hernia, diaphragmatic ... 705, 784, 828
duodenal ... 814
hiatus, recurrent ... 170
Hexamethylenamine in cholecystitis ... 22
"Hiatus hernia" syndrome ... 170
Histamine, and gastric secretion ... 787
in blood ... 248
in dog's stomach ... 248
Histopathology, anal crypts ... 146
Hog's stomach, in achlorhydria ... 543
Hollander hypothesis of gastric juice ... 327
Hunger, gastric mechanism ... 688
Hydration, of body ... 126
Hydremia ... 116
Hydrops, of gall bladder ... 19, 22
Hyperinsulinemia ... 64
Hyperinsulinism ... 797
types of ... 562
Hyperparathyroidism ... 865
Hypertension, in adiposity ... 251
in migraine ... 16
Hysteria ... 671
due to hyperinsulinism ... 563

Ileitis, distal ... 783
familial ... 98
regional ... 97
regional enteritis ... 161
terminal ... 426, 552
Ileostomy ... 190
Ileus, acute ... 271
Index, icterus ... 22, 105
Infection, foci, in colitis ... 191
gall bladder ... 759
pelvic ... 611
Infestation of gall bladder ... 22
parasitic of gall bladder ... 20
protozoal ... 115
Inheritance, in gastrointestinal disease ... 480
Innervation, gastrointestinal ... 845
sympathetic secretory of gastric mucosa ... 36
Insanity, equivalents ... 307
familial ... 307
Insulin, in peptic ulcer ... 135
Insulin secretion, anomalies of ... 115
Intestinal, intubation ... 248
obstruction in amebiasis ... 228
perforation in amebiasis ... 228
tuberculosis, diagnosis of ... 303
treatment of ... 303
ulceration ... 297
due to amebic infestation ... 298
Intestine, cancer of ... 588, 808
obstruction of small ... 92
Intussusception ... 189
Iodamoeba, buetschlii ... 4
williamsi ... 457
Iodine, in colitis ... 191
Irradiation of exposed stomach ... 164

Irrigation, colonic ... 397
intestinal ... 190
Irritable stomach ... 553
Isospora hominis ... 457

Jaundice ... 314
in arthritis ... 259
with ascites ... 113
catarrhal ... 553
in syphilis ... 173
obstructive ... 104
Jejunum, diverticula of ... 708
Juice, gastric, in anemia ... 677

Lamblia, in gall bladder ... 23
Lambliasis cholecystitis ... 233
"Law of intestine" ... 245
Leishmania braziliensis ... 457
donovani ... 457
tropica ... 457
Lesions, pre-cancerous ... 222
Leukoplakia ... 222
Ligament, cysto-colic ... 197
gastro-hepatic ... 197
hepato-colic ... 197
hepato-duodenal ... 197
reno-colic ... 197
Lipase, blood ... 707
role of ... 448
Lipoid metabolism, liver in ... 179
Lipoma of colon ... 402
Liver, abscess ... 228
cirrhosis of ... 315, 554
disease in pernicious anemia ... 256
extract, canine ... 116
function tests ... 225, 505
intraveous galactose ... 310
histology in peptic ulcer ... 537
tropical ... 31
tumors, hematemesis in ... 553
Lobster, effect on gastric juice ... 181
Loops, of colon ... 722
Lymphoid tissue, amebic invasion of ... 32

Magenstrasse ... 30
Magnesium sulphate (experimental) ... 176
Maltase, in duodenal fluid ... 622
Management, of anal fissure ... 144
ulcerative colitis ... 190
Mechanics, of G. I. tract ... 248
Mechanism, of hunger ... 688
Megacolon, experimental production of ... 33
Membrane, congenital pericolic ... 196
Jackson's ... 197
Meniscus sign in gastric cancer ... 370
Mesentery, chycle cysts of ... 34
Lane's "false" ... 197
Metabolism, early studies ... 50
in arthritis ... 438
lipoid ... 798
Metal poisoning ... 671
Metastases, pelvic ... 611
Migraine ... 14
new aspect of ... 359
Minerals ... 44
Mortality, in appendicitis ... 477
in diabetic children ... 180
in rectal cancer ... 141
Motility, of gall bladder ... 174
gastric ... 373
Mucilaginous substances ... 684
Mucin ... 869
causing uremia ... 192
gastric ... 177
Mococele, of gall bladder ... 22

Mucoitin ... 178
Mucosa, gastric destruction by X-ray ... 164
gastric sympathetic innervation of ... 36
Mucus in stools ... 298
Myoma, of colon ... 401
Myosarcoma, of stomach ... 825

Narcolepsy and hyperinsulinism ... 567
Nausea ... 101
in gall bladder disease ... 293
in migraine ... 16
Neoplasm, causing obstruction of duodenum ... 92
of gall bladder ... 19
malignant of gall bladder ... 22
non-malignant of gall bladder ... 22
Nephritis ... 47
Nervous manifestations, due to balantidiosis ... 305
due to syphilis ... 305
due to vitamin lack ... 305
seen by gastroenterologist ... 305
Nervous phenomena in gall bladder disease ... 292
Neuritis in ulcerative colitis ... 467
Niche in peptic ulcer ... 516
Nocturnal gastric secretion ... 778
Novacaine (experimental) ... 175
Nursing in amebiasis ... 32
Nutrition, early views ... 49
in chronic arthritis ... 438
in health and disease ... 44
in pernicious anemia ... 857

Obesity ... 250
treatment of ... 578
Obstruction, acute intestinal ... 63
cystic duct ... 21
duodenum ... 92
intestinal ... 185
intestinal in colonic cancer ... 585
of jejunum (experimental) ... 64
pyloric ... 589
small bowel ... 271
small intestine ... 589
upper portion of small intestine ... 92
Oesophagus, artificial ... 33
"Okrin" in peptic ulcer treatment ... 713
Operation, cancer of colon ... 885
cancer of rectum ... 885
gastric, anemia following ... 829
Opium, camphorated tr. in colitis ... 191
Overfeeding, in anemia ... 131
Oxygen pressure effect on gastric motility ... 373
Oxytocin (experimental) ... 175

Pain, abdominal ... 244
high rectal ... 591, 899
in peptic ulcer ... 94
in regional ileitis ... 427
Pancreas, annular ... 888
cancer of ... 707
diseases of ... 871
physiology of ... 445
Pancreatitis, acute ... 64, 871
causing obstruction ... 93
medical treatment of ... 441
subacute ... 443
subacute and dysinsulinism ... 565
Papaverine ... 248
(experimental) ... 175
Papillomas of colon ... 403
Paraffinomas of colon ... 403
Parasitic ... 351
Parasites, in pernicious anemia ... 863
Parathormone, in colitis ... 191
Pathology, of pernicious anemia ... 860
Pectinosis ... 821

Pellagra 93
digestion and absorption in..... 431
in giardiasis..... 769
secondary 244
treatment with liver..... 259
Pelvic disturbances..... 609
Pepsin 617
affected by mucin..... 178
and pH..... 120
Peptic ulcer, alkalosis in treatment of..... 509
aluminum hydroxide in treatment..... 513
and trauma..... 552
bacterial vaccines in..... 338
blood tests in..... 834
cure by surgery..... 137
familial incidence..... 75
healing of..... 516
liver in..... 537
treatment by insulin..... 135
treatment for..... 522
Peptone (experimental)..... 176
Perforation of colon..... 883
Peritonitis 64
biliary 140
Pernicious anemia..... 240
dietary phases..... 131
digestion and absorption in..... 431
experimental 116
gall bladder disease in..... 256
nutritional aspects of..... 857
racial factor in..... 259
treatment 184, 398, 628
Phenomenon, Arthus..... 30
Phenophthalein 21
Phospholipoids 617
Phrenicectomy, unilateral..... 471
Physiology, of G. I. innervation..... 845
of pancreas..... 445
Pigment, absorption of..... 123
Pilocarpine, and gastric secretion..... 789
(experimental) 174
Pitressin (experimental)..... 174
Pituitary, in hypertension..... 259
Pituitrin (experimental)..... 174
Plasmodium falciparum..... 457
malariae 457
vivax 457
Penumonia and acute abdomen..... 188
Pneumoperitoneum 645
Poisoning, cinchophen..... 29
Polyp, of colon..... 821
of rectum..... 141
single gastric..... 169
of stomach..... 34
Polyposis, of colon..... 695
of duodenum..... 755
of jejunum..... 755
Portal thrombosis, bland..... 500
Portal vein, diseases of..... 498
Postoperative management of gall bladder cases..... 25
Power, bactericidal of stomach..... 725
Pregnancy, and insulin..... 259
Preoperative preparation of gall bladder cases..... 25
Pressure, abdominal arterial..... 561
intracranial 853
Procidentia, recti..... 63
Proctitis 101
treatment of..... 816
factitial 592
obliterans 142
Prophylaxis, of common cold..... 795
Prostate, disease of..... 593
Proteins, digestion in man..... 383
native 617
unchanged in transfused blood..... 891
Protozoa, pathogenic in U. S. A..... 456
Pruritis ani..... 15, 101
Pseudo-polyposis 161
Psychology of gall bladder..... 290
Psychopathic patient, the..... 306
Psychosis from hyperinsulinism..... 564
Pus in stools..... 298
Pyloric obstruction..... 554
Pylorospasm 173
Pylorostenosis 173
Pylorus, influence on acidity..... 245
Pyrosis 101

Quinoline drugs in gall bladder disease..... 18

Racial factor in pernicious anemia..... 259
Radiograms in amebiasis..... 32
Rectocele 593
Rectum, cancer of..... 881
high pain in..... 591
impalement of..... 604
stricture of..... 594
surgery of..... 66
Reflex, conditioned..... 845
gastro-ileo-colic 851
mesenteric 245
Rennin and pH..... 120
Retortamonas intestinalis..... 457
Roentgenology in peptic ulcer..... 52
Rosemann theory of gastric juice..... 321

Salyrgan, in adiposity..... 253
Sarcocystis sporozoon..... 457
Scars, of ulcer..... 139
Scurvy, heart in..... 259
Secretion, effect of histamine..... 787
gastric 627
and sympathetic nervous system..... 40
and vitamin deficiency..... 244
chemical phase of..... 715
histamine in..... 561
nocturnal 778
of small bowel..... 179
pancreatic 794
Sepsis after abdominal disease..... 404
Sera, in colitis..... 190
Serum, for colitis..... 582
staphylococcus 870
Sigmoid, cancer of..... 738
diverticulitis of..... 738
Sinuses in gall bladder disease..... 295
Small intestine, chronic inflammatory lesions of..... 426
Sodium bicarbonate..... 21
chloride (experimental)..... 175
glycocholate 21
oleate 21
salicylate 21
thiocyanate test..... 126
Sour stomach..... 101
Spasm, in peptic ulcer..... 63
Specific dynamic action..... 50
Specificity, test in amebiasis..... 548
Sphincter, Oddi's..... 20
Spider bite..... 318
Spinal cord, subacute combined degeneration..... 560
Stasis, duodenal..... 92
Steatorrhea 173
Stimulation of organs..... 853
Stomach, bactericidal power of..... 725
cancer of..... 814
desiccated of dog..... 116
emptying 684
functional disorder..... 773
myosarcoma of..... 825
post-operative 742
syphilis of..... 822
thoracic 554
X-ray of..... 260

Stone, in common duct ... 312
urinary tract ... 188
Stones, "metabolic" ... 222
Streptococci ... 223
in experimental cholecystitis ... 759
in pernicious anemia ... 256
Streptococcus perirectal cellulitis ... 413
viridans ... 291
Stricture, of intestine ... 802
of rectum ... 142
Sugar, blood ... 834
Substances, *mucilaginous* ... 684
Suprarenal glands ... 737
Surgery, abdominal ... 60
biliary ... 140
biliary tract ... 270
of gall bladder ... 140
plastic of colon ... 66
Sympathectomy in megalocolon ... 408
Symptoms, of duodenal cancer ... 840
of pernicious anemia ... 857
referred ... 554
Syndrome, congenital pericolic membrane ... 196
Felley's ... 244
unusual in common duct stone ... 312
von Bergmann's ... 170
Syphilis, gastric ... 408, 589
in gall bladder disease ... 19
of esophagus ... 802
of gall bladder ... 22
of stomach ... 822
tertiary ... 69
System, digestive in pernicious anemia ... 857

Tachycardia and hyperinsulinism ... 563
Technique for X-ray of hiatus hernia ... 171
special in X-ray ... 52
Temperature, G. I. tract ... 115
Teratoma of colon ... 402
Test, Aldrich ... 24
bromsulphalein dye ... 24
complement fixation, in amebiasis ... 548
cutaneous for food allergy ... 102
fat tolerance ... 834
functional, of liver ... 505
galactose ... 24
galactose tolerance in pernicious anemia ... 258
hay ... 24
for hydration ... 126
index, icterus ... 24
neutralization ... 242
of blood for enzymes ... 732
Pettenkofer ... 24
urobilinogen ... 24
van den Bergh ... 105, 22
Widal's hemoclastic shock ... 24
Tetany ... 93
Tetraiodophenolphthalein ... 174
Theory endogenous, of adiposity ... 250
Therapy ... 58
Thrombosis, suppurative, of portal vein ... 498
Thymus extract ... 818
Thyroid, ablation of ... 865
Tinkle, metallic ... 883
Tissue, pancreatic in stomach wall ... 34
Titration of gastric juice ... 330
Tobacco, in functional disease ... 776
Tolerance, fat ... 834
Tongue, coated ... 101
Toxemia, in obstruction ... 96
Tract, alimentary, functional disorder of ... 773
Transfusions, in chronic colitis ... 191
Trauma, by enema ... 207
Treatment, amebiasis ... 487
functional vomiting ... 635
injection ... 63
medicinal for amebiasis ... 147
of acute cholecystitis ... 22
of diverticulitis ... 193
of functional disease ... 776
of gall bladder disease ... 221
of hemorrhage ... 803
of migraine ... 17
of obesity ... 578
of pancreatitis ... 871
of peptic ulcer ... 520
a rationale for ... 522
of pernicious anemia ... 184
portal cirrhosis ... 810
ulcerative colitis ... 190
Tree, normal biliary ... 106
Treparsol ... 13
Trichomonas buccalis ... 457
vaginalis ... 457
Trichuris ... 768
Trypanosoma cruzi ... 457
gambiense ... 457
rhodesiense ... 457
Trypsin, estimation of ... 248
inactivation of ... 248
Tube, duodenal in intestinal obstruction ... 63
Tuberculosis of gall bladder ... 22
in gall bladder disease ... 19
Tumors, benign of stomach ... 140
inflammatory ... 783
of colon and rectum ... 146
of stomach ... 581
pelvic ... 592, 612
pituitary and peptic ulcer ... 34
uncommon, of large intestine ... 400
Typhoid in gall tract disease ... 18

Ulcer-cancer problem ... 244
Ulcer, duodenal ... 645
and polycythemia ... 244
surgery in ... 137
X-ray in ... 578
gastric ... 29
diagnosis and prognosis ... 697
mucin in and atropine in ... 34
streptococcus of ... 33
surgery in ... 137
gastrojejunal ... 526
jejunal ... 272, 802
luetic, of stomach ... 868
of diverticulum ... 814
pain in ... 173
peptic ... 75
and pituitary tumor ... 34
conservative surgery ... 262
cure by surgery ... 137
etiology ... 244
medical aspects ... 866
perforated ... 134, 187
treatment by insulin ... 135
role of infection in ... 33
production mechanism of ... 297
scars ... 139
silent ... 30
treatment by short wave ... 806
Ulceration, intestinal ... 297
intestinal bleeding in ... 297
due to bacillary dysentery ... 301
intestinal due to neoplasm ... 304
due to typhoid ... 304
due to tuberculosis ... 303
tuberculous of rectum ... 70
Ulcerative colitis ... 466
idiopathic ... 302
Uremia, digestive tract changes in ... 552

Vaccine, in cholecystitis ... 22
in chronic ulcerative colitis ... 190

Vagotonia 135
Ventriculin in experimental amebiasis..... 627
Vioform 13
Vision in gall bladder disease..... 291
Vital capacity, in adiposity..... 251
Vitamins 45, 420
A, in common "cold"..... 795
C 868
ABCDE 46
in tuberculosis..... 259
Vomiting 101
functional 635
in gall bladder disease..... 293
in migraine..... 16
prolonged 671
von Bersmann's syndrome..... 170

Water 45
absorption 376
balance 589
estimation in disease..... 132
metabolism in migraine..... 362
retention in adiposity..... 253

X-ray destruction of gastric mucosa..... 164
factors of error..... 260
in duodenal ulcer..... 579
in regional ileitis..... 429
in acute abdomen..... 185
technique for hiatus hernia..... 171

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for Peptic Ulcer



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